CHRONIC DISEASE PROFILE OF PLHIV ON LONG TERM

ANTIRETROVIRAL THERAPY

A dissertation submitted in partial fulfilment of the rules and regulations for MD General Medicine examination of the Tamil Nadu Dr.M.G.R Medical University, Chennai, to be held in May, 2018.

DECLARATION

This is to declare that this dissertation titled —"Chronic disease profile of PLHIV on long term antiretroviral therapy"is my original work done in partial fulfilment of rules and regulations for the MD General Medicine examination of the Tamil Nadu Dr.M.G.R Medical University, Chennai to be held in May, 2018.

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CERTIFICATE

This is to declare that this dissertation titled ―"Chronic disease profile of PLHIV on long term antiretroviral therapy" is a bonafide work done by Dr Sumayya Abdul Kalam in partial fulfilment of rules and regulations for the MD General Medicine examination of the Tamil Nadu Dr.M.G.R Medical University, Chennai to be held in May, 2018

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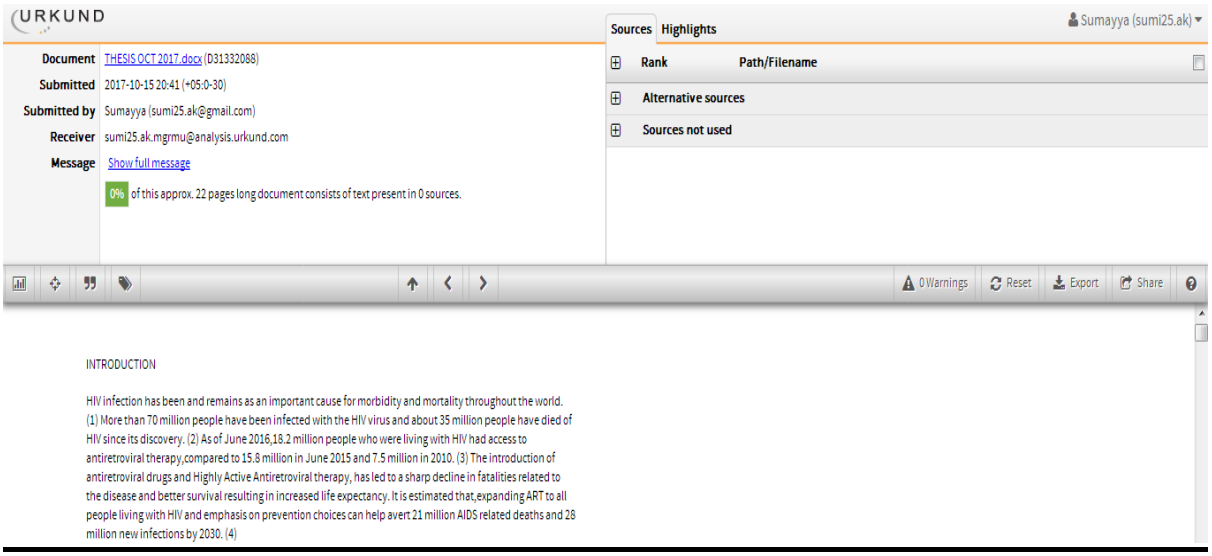
Above all, I acknowledge the loving and encouraging presence of the Almighty which spurred me on to tirelessly and energetically complete this thesis.

ANTIPLAGIARISM CERTIFICATE



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Contents

1.INTRODUCTION

HIV infection has been and remains as an important cause for morbidity and mortality throughout the world.(1) More than 70 million people have been infected with the HIV virus and about 35 million people have died of HIV since its discovery.(2) As of June 2016,18.2 million people who were living with HIV had access to antiretroviral therapy,compared to 15.8 million in June 2015 and 7.5 million in 2010.(3) The introduction of antiretroviral drugs and Highly Active Antiretroviral therapy, has led to a sharp decline in fatalities related to the disease and better survival resulting in increased life expectancy. It is estimated that,expanding ART to all people living with HIV and emphasis on prevention choices can help avert 21 million AIDS related deaths and 28 million new infections by 2030.(4)

HIV/AIDS is a growing global problem, in terms of incidence and mortality. Patients with HIV are living much longer with HAART so much so that HIV has now become a part of the chronic disease burden, like hypertension or diabetes.(5) However adverse metabolic effects like dyslipidemia, increased blood pressure and insulin resistance have been attributed to HAART. Therefore the use of HAART rises concerns regarding metabolic disorders and cardiovascular risk in HIV infected patients who now present an extended life expectancy.(6)

In view of the increased longevity attainable with the current therapy for HIV, quality of life of people living with HIV also becomes a significant issue to be considered in this context; it becomes an important medical outcome measure and its improvement in all domains becomes a targeted goal as part of overall management of HIV.(7)

2.AIM OF THE STUDY

To study the profile of chronic diseases among HIV patients who have been on long term antiretroviral therapy in a tertiary care centre in South India.

3.OBJECTIVES OF THE STUDY

Primary Objective

To study the profile of chronic diseases among patients with HIV on long term antiretroviral therapy.

Secondary Objectives

1. To assess the adequacy of treatment of diabetes, hypertension and dyslipidemia as per standard guidelines in the same population.

2. Assessment of cardiovascular risk in the same population.

3. Assessment of quality of life in the same population.

4.LITERATURE REVIEW

4.1 PATHOPHYSIOLOGY

The multiple mechanisms by which PLHIV on HAART become more susceptible for development of chronic diseases is via the effect of chronic inflammation produced by the virus per se as well as side effect profile of the drugs that constitute Highly Active Antiretroviral Therapy(HAART) .Moreover the increased life expectancy offered by HAART contributes to the increased incidence of metabolic and cardiovascular diseases.

HIV and atherosclerosis

Atherosclerosis is found to occur and progress at a faster rate in patients with HIV infection when compared to HIV non infected individuals.(8)

1. HIV infected individuals have been found to have increased levels of triglycerides and decreased levels of HDL cholesterol.(9)

2. A major role is also played by chemokines both in the occurrence of HIV infection and progression to atherosclerosis due to HIV and genetic variations in them has been found to cause the same.(10)Chemokines play a role in both the entry of HIV into the cell as well as the ability of monocytes to enter the subendothelial space which is an important step in development of atherosclerosis. Mononuclear phagocytes (monocytes

and macrophages) are primarily involved in the inflammatory processes in the development of atherosclerosis. MCP 1(Monocyte Chemoattractant Protein 1) is a chemokine which mediates attraction of circulating monocytes to subendothelial space via its receptor CCR2.(8) These monocytes phagocyte lipoprotein and form lipid laden foam cells. A mutation which causes overexpression of MCP 1 has been found to be associated with higher rates of atherosclerosis.(11).Another molecule is Stromal Derived Factor 1(SDF 1) which causes activation of platelets within the atheromatous plaque and enables smooth muscle cell migration into subendothelial space.Polymorphisms leading to lower expression of this molecule is associated with delayed progression to atherosclerosis.(8) Fractalkine is yet another chemokine which is upregulated in inflamed tissues.It serves as a chemoattractant as well as adhesion molecule. DNA polymorphisms in the gene for its specific receptor CX3CR1 have been implicated in atherosclerosis.(12)

3. It has also been found that higher CD4 counts relate to slower rates towards atherosclerosis and similarly low CD4 counts as a significant risk factor for increased subclinical atherosclerosis.(13).

4. HIV-1 infection is implicated in hampering insulin sensitivity. The HIV-1 accessory protein Vpr has been found induce transcription of glucocorticoid-responsive promoters, thereby increasing sensitivity to glucocorticoids . It also diminishes peroxisome-proliferator-activated receptor-γ (PPAR-γ) activity and interferes with the

inhibitory effects of insulin on forehead transcription factors. Hence, tissue-selective insulin resistance is produced.(14)

HAART and atherosclerosis

The role of antiretroviral agents,particularly protease inhibitors in causing dyslipidemia has been widely studied.

The proposed mechanisms include:(15,16)

1. The activation of sterol regulatory element-binding protein-1 (SREBP-1) is inhibited in the liver and adipocytes along with the protease mediated breakdown of apolipoprotein-B.

2. Upregulation of very low density lipoproteins (VLDLs) formation.

3.Decrease in the lipoprotein lipase activity .

4. Altered mobilization of lipid stores.

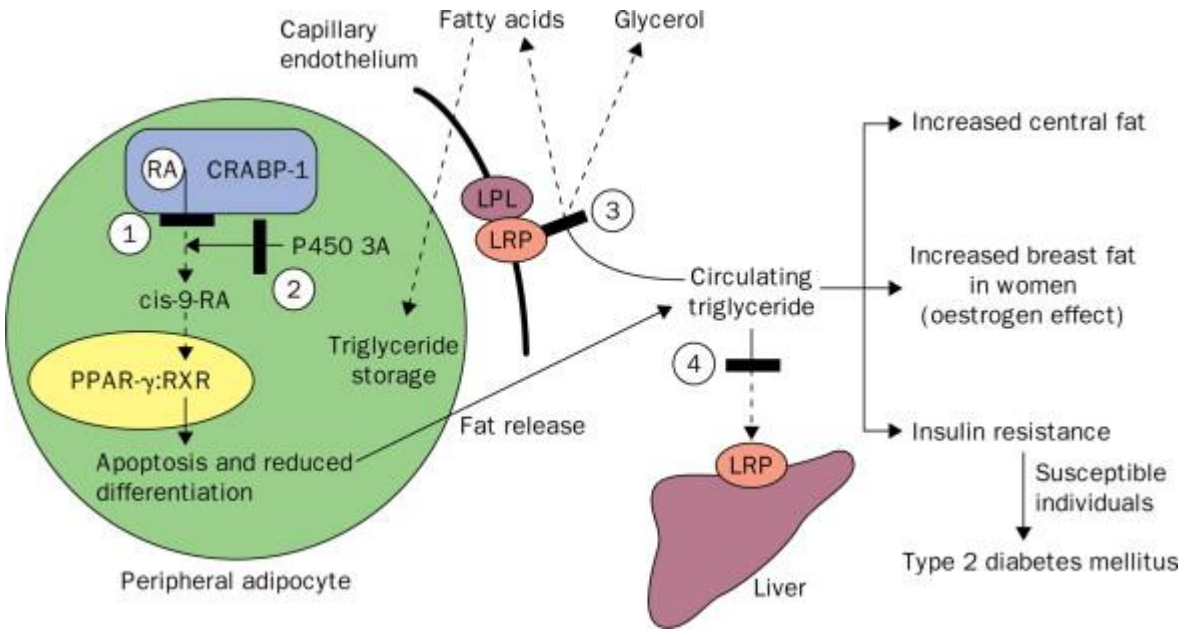
Antiretroviral therapy other than those containing protease inhibitors have also been found to cause lipid disorders.(17)

The mechanisms by which ART,especially protease inhibitors cause hyperlipidemia,lipodystrophy,central obesity and insulin resistance include:

1.Inhibition of insulin mediated glucose uptake in adipocytes in a dose dependent manner by decreasing the intrinsic transport activity of GLUT4 isoform,which is an insulin regulated glucose transporter.(18)

2. CRABP 1(Cytoplasmic Retinoic Acid Binding Protein 1) is a protein that binds to retinoic acid and presents it to cytochrome P 450 which is the enzyme which converts retinoic acid to cis 9 retinoic acid,which in turn is the only ligand for retinoic X receptor(RXR). RXR works as a heterodimer with peroxisome-proliferator-activated receptor type gamma (PPAR-γ). Ligand binding to RXR or PPAR-γ inhibits adipocyte apoptosis and favours adipocyte differentiation and proliferation and PPAR gamma acts preferentially on peripheral fat.(19)

Protease inhibitors can act on all the above said steps as depicted in the figure below.



Protease inhibitors either directly bind to CRABP 1 or inhibits cytochrome P450 3A which causes decrease in the amount of cis 9 retinoic acid .This reduces retinoic X receptor (RXR) stimulation thereby causing decreased apoptosis and impaired differentation of peripheral adipocytes, with lipid release and/or reduced lipid storage.

3. LDL receptor related protein (LRP) is a hepatic receptor which is crucial for post-prandial chylomicron clearance. LRP is also co-expressed on capillary endothelium with lipoprotein lipase (LPL). The LPL-LRP complex allows free fatty acid to enter into fat cells by cleaving fatty acids from circulating triglycerides and thereby permits fat storage. Protease-inhibitor binding of hepatic and endothelial LRP would result in increased lipid levels in blood and decreased fat storage via reduced cleavage of fatty acids from circulating triglycerides and reduced hepatic uptake of chylomicrons .(20) The resulting hyperlipidemia causes fat redistribution to the abdomen as well as in the breasts as central adipocytes are metabolically more active than peripheral ones,hence central fat accumulation automatically results when peripheral fat storage mechanisms are impaired.

4. Increased lipid levels by the above mechanisms leads to insulin resistance by:(21)

   a. interference with post-receptor insulin signalling

   b. competition between glucose and lipid oxidation pathways in skeletal muscle (Randle's cycle)

   c. Inhibition of glycogen synthase

5.There has been recent progress in elucidating the role played by adipokines in HIV and HAART induced atherosclerosis.

4.2EPIDEMIOLOGY

GLOBAL BURDEN

The worldwide prevalence of cardiovascular risk factors like insulin

resistance,dyslipidemia and hypertension among people living with HIV and who has been on HAART has been found to range from 13-45%.(22,23). In a study conducted in Brazil to assess prevalence of dyslipidemia, cardiovascular risk and metabolic syndrome in a group of HIV patients with and without HAART

separately,it was found that metabolic syndrome was prevalent in 3% of those on

HAART and 12% of those not on HAART respectively.Total and HDL cholesterol, triglycerides and blood glucose were found to be higher in the HAART pool than among the non HAART pool. Cardiovascular risk associated with HAART is reported to be moderate (11%) vs 4% without ART. (24)

A systematic review published in 2017 revealed a range of 8.4% to 47% rate of metabolic syndrome in HIV positive patients. The same review showed an average prevalence of 21.5% in Asia and 30.5% in Africa(25)

In another study which aimed to look at the cardiovascular risk factors in HIV patients on long term HAART,40% of individuals were found to have high levels of total cholesterol.

Patients who were on HAART had 8 times risk of developing hypercholesterolemia as compared to those not on HAART with

an odds ratio of 8.17.Hypertension occurred twice in the HAART population as compared to HAART naïve population,with a prevalence of 25.6%.Cardiovascular disease risk was significantly high in patients treated with HAART for more than 5 years.(26)

INDIAN BURDEN

The scenario in India is no less different.

In a study conducted in South India ,it was found that a high prevalence of metabolic syndrome was observed in patients with HIV (16/60), and was more prevalent in

the ART-treated group (13/30; P = 0.028). Similarly, insulin resistance was also noted to be high (24/60), and of these patients, 15 were on ART. Seventy-five

percent of patients with metabolic syndrome had insulin resistance.

All the patients satisfied at least one component of metabolic syndrome.(27)

The data from another Indian study show that metabolic abnormalities like hypercholesterolemia,hypertriglyceridemia,low HDL,hyperinsulinemia and truncal adiposity were clustered in HIV infected patients with fat redistribution.(28)

Table: 3. Assessment of risk of hypertension, impaired glucose tolerance, diabetes, and dyslipidemia of patients infected with human immunodeficiency virus with and without lipodystrophy (case patients) and control subjects

Variable	Lipodystrophy patients		Without lipodystrophy patients	
	HIV-infected patients, %,	Control subjects, %	HIV-infected patients, %,	Control subjects, %
Systolic BP >140 mm Hg	4.2	5.2	6.7	3.3
Diastolic BP >90 mm Hg	11.3	5.6	6.7	1.1
Fasting insulin level >18 mU/mL	26.5	6.1	3.5	2.2
2-h glucose level >200 mg/dL	7.0	0.5	5.6	0.4
IGT (2-h glucose level >140 mg/dL)	35.2	5.2	5.6	3.3
Cholesterol level .>200 mg/dL	57.1	41.8	16.7	30.0
Triglyceride level >200 mg/dL	57.1	8.9	13.3	5.6
LDL level >160 mg/dL	21.8	14.1	6.9	4.4
HDL level <35 mg/dL	45.7	16.9	43.3	5.6

NOTE: *BP, blood pressure; HDL, high-density lipoprotein; IGT, impaired glucose tolerance; LDL, low-density lipoprotein.*

Another Indian study which assessed 70 HIV positive patients showed that the prevalence of metabolic syndrome was 20%. Majority of patients had only one component of metabolic syndrome (32.9%). Low HDL was present in 50%, followed by raised triglycerides in 42.9%. Waist circumference was not increased in any of the patients. There was no statistically significant difference between those on HAART and those not on HAART in distribution of risk factors and individual components of metabolic syndrome.(29)

Another study in Western India showed that of the 306 patients assessed in the study,the prevalence of lipodystrophy was 46.1%, and lipoatrophy was significantly associated with Stavudine use. The prevalence of dyslipidemia and fasting hyperglycemia was significantly higher in the treatment groups. Proportion of patients with high-density lipoprotein > or = 60

mg/dL was significantly higher in the treatment groups; however, this did not have much impact on the total cholesterol to HDL ratio .(30)

In a study conducted in our hospital to assess the prevalence of cardiovascular risk factors in patients on antiretroviral therapy for a period of 1 year,it was found that the prevalence of dyslipidemia was found to be statistically significant when patients on ART were compared with ART naive patients.34% of patients on ART were found to have high LDL values as compared to 17.2% in ART naïve patients.(31)

Review of literature for chronic disease profile among PLHIV on ART is as follows:

4.3 DIABETES MELLITUS

HIV/AIDS patients frequently present with diabetes and related metabolic complaints.As lifespan on ART increases,and access to therapy improves,HIV related diabetes is expected to increase. A higher risk of insulin resistance and diabetes mellitus has been described in HIV-infected patients on ART compared with HIV uninfected patients.

14% ,that is,57 of the 411 males who were HIV infected and using HAART at the baseline visit had prevalent DM compared with 5%,which is 33 of the 711 HIV-seronegative men (prevalence ratio = 4.6; 95% confidence interval, 3.0-7.1, adjusted for age and BMI. The rate of incident diabetes was found to be 4.7 cases per 100 person years among HIV-infected men using antiretroviral therapy compared with 1.4 cases per 100 person years among HIV-

uninfected men during the four-year period of observation in the Multicenter AIDS Cohort Study.(32)

Table 1. Characteristics of 1278 Men at the Index Visit Between April and October 1999*

Characteristic	MACS (n = 5622)	Current Study Population (N = 1278)	HIV-Seronegative (n = 710)	HIV-Infected Not Using HAART (n = 157)	HIV-Infected Using HAART (n = 411)	*P* Value†
White subjects, No. (%)	4681 (83)	1089 (85)	618 (87)	119 (76)	352 (86)	.53
College degree, No. (%)	3121 (56)	787 (62)	477 (67)	74 (47)	236 (57)	<.001
Age (IQR range), y	33 (28, 38)	48 (43, 53)	50 (45, 56)	46 (41, 50)	46 (42, 51)	<.001
Body mass index‡	23 (22, 25)	26 (24, 28)	26 (24, 29)	25 (23, 28)	25 (23, 27)	<.001
Waist-hip ratio	NA	0.95 (0.91, 0.99)	0.94 (0.90, 0.99)	0.94 (0.91, 0.97)	0.95 (0.91, 0.99)	.17
Total cholesterol level, mg/dL	NA	202 (176, 229)	201 (178, 227)	188 (158, 218)	210 (182, 239)	<.001
Glucose level, mg/dL	NA	90 (83, 98)	90 (83, 97)	88 (82, 98)	91 (84, 101)	.03
Nadir CD4 count, cells/mm^3	NA	NA	NA	318 (187, 432)	211 (108, 318)	NA
Duration of receiving HAART§	NA	NA	NA	NA	3.26 (2.63, 3.81)	NA

Abbreviations: HAART, highly active antiretroviral therapy; HIV, human immunodeficiency virus; IQR, interquartile range; MACS, Multicenter AIDS Cohort Study.
SI conversion factors: To convert total cholesterol to millimoles per liter, multiply by 0.0259; glucose to millimoles per liter, multiply by 0.0555.
*Data are given as medians (interquartile range), unless otherwise indicated.
†Compared HIV-infected receiving HAART group with the HIV-infected group, by the Fisher exact test or the Wilcoxon nonparametric test, as appropriate.
‡Calculated as weight in kilograms divided by the square of height in meters.
§Years from initiation of HAART to the date of index visit.

Yet another multicentre cohort study which assessed the development of new onset diabetes with exposure to antiretroviral therapy revealed a diabetes incidence of 5.72 per 1000 person years of follow up and it increased with cumulative exposure to ART.A remarkable finding was that exposure to stavudine had the most significant association for development of new onset diabetes.Other drugs which were implicated with risk of new onset diabetes were zidovudine and didanosine.Interestingly,exposure to ritonavir and nevirapine were associated with reduced risk of developing diabetes.(33)

In the Swiss HIV Cohort Study, risk factors for type 2 diabetes were assessed and the same was published in 2007 in Clinical Infectious diseases. 4.4 cases per 1000 person years of

follow up was the incidence of diabetes calculated.The risk factors identified for increased incidence of diabetes were:

1. Male gender
2. Age more than 60 years
3. Black race
4. Asian ethnicity
5. CDC stage C
6. Obesity
7. Current treatment with NRTIs, NRTIs with PIs

Treatment with NNRTis were not found to be associated with development of diabetes.(34)

The current recommendations advise to check HbA1c and/or fasting blood glucose at the following timelines in HIV patients :

1. baseline
2. prior to initiating ART
3. within one to three months after starting a new regimen
4. every three to six months thereafter while on ART

The target HbA1c should be maintained at less than 7% for adequate control.(35)

It has also been found that the HbA1C level may underestimate fasting glucose in HIV-infected patients. In the Multicenter AIDS Cohort Study where 3000 individuals were assessed, at a given fasting glucose level ≥125 mg/dL, the concomitant HbA1C was lower in HIV-infected individuals as compared with uninfected individuals. Lower CD4 cell counts and HAART use were independently associated with a lower HbA1C level than expected for the fasting glucose level.(36)

Strict screening and monitoring must be ensured to make sure that diabetes is not left undetected in the HIV population and once diagnosed,the goal should be to achieve glycemic control as per target guidelines so as to minimise the cardiovascular risk and thereby prevent further complications.

4.4 SYSTEMIC HYPERTENSION

Hypertension is another leading lifestyle disease which can act as the "killer disease" in many circumstances and it is important to know how HIV positive patients are at increased risk for the same.

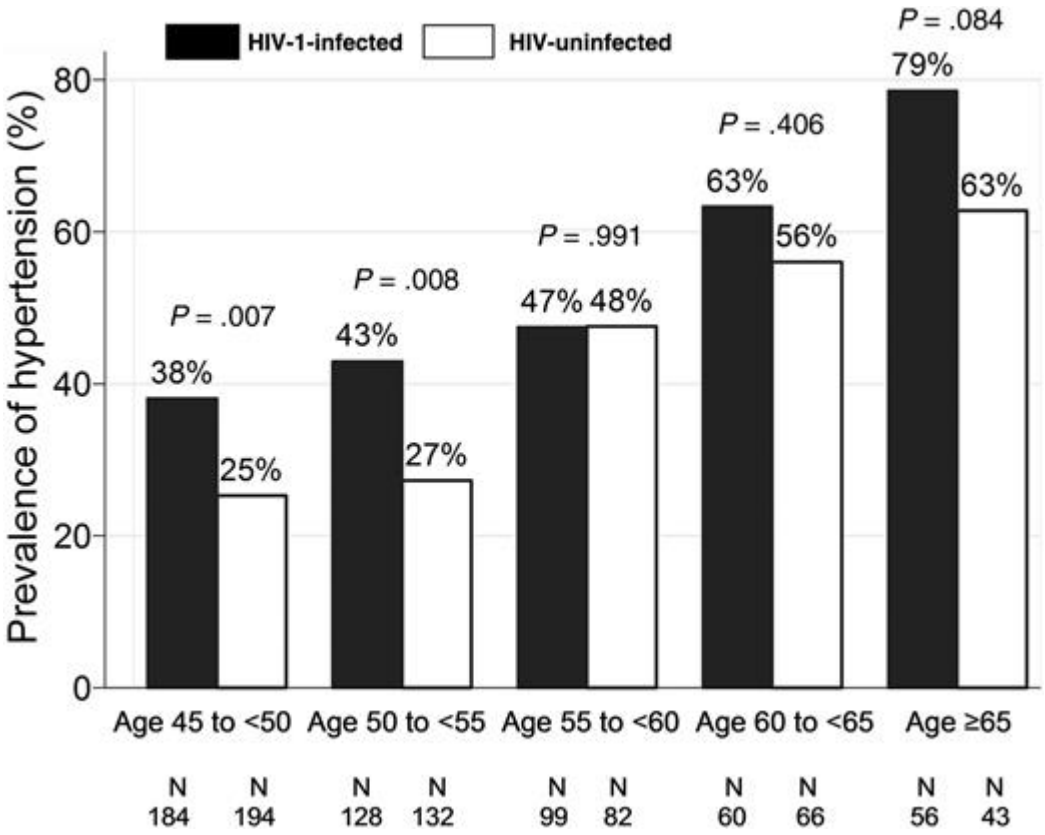
In a study conducted in Limbe Regional Hospital HIV treatment center in Cameroon between April and June 2013, involving 200 HIV/AIDS patients it was found that the prevalence of hypertension was double in HIV patients on HAART as compared to those not on it(38% vs 19%).(37)

In the Multicentre AIDS Cohort Study which was done to look at the impact of HIV infection and highly active antiretroviral therapy on systolic and diastolic hypertension,it was found that 7.3% had systolic hypertension and 8% had diastolic hypertension.Men taking highly active antiretroviral therapy (HAART) for less than 2 years had similar rates of systolic hypertension to that among HIV negative men (OR, 1.06; 95% CI,0.87–1.30), but was significantly higher thereafter, for 2 to 5 years of HAART and for more than 5 years of HAART.

But the converse was not true. Diastolic hypertension was not significantly higher among men with prolonged HAART use compared to that among HIV negative controls.(38)

In another study done by the AGEhiV Cohort study group, the prevalence of hypertension was 48.2% in HIV infected and 36.4% in HIV-uninfected individuals with an odds ratio of 1.63; 95% CI, 1.27–2.09; $P < .001$). Across all ages, the prevalence of hypertension was higher in HIV infected patients. Seropositive individuals received significantly more antihypertensive treatment (22.8%) compared with HIV negative individuals (13.9%; $P < .001$) and had a comparable rate of hypertension control.Also, among HIV 1infected individuals, stavudine exposure was independently associated with hypertension (OR, 1.54; 95% CI, 1.04–2.30). This association was attenuated after additional adjustment for either waist-to-hip ratio (OR, 1.30; 95% CI, .85–1.96) or hip circumference (OR, 1.40; 95% CI, 0.93–2.11).

Hence the study suggested that changes in distribution of body fat composition, involving both abdominal obesity and stavudine-induced peripheral lipodystrophy, might contribute to the higher prevalence of hypertension in HIV infected patients.(39)



A systematic review published in 2015 looked at the following aspects in HIV infected individuals pertaining to hypertension.

1. Severity of HIV vs hypertension

2. Duration of HIV vs hypertension

3. Type of ART vs hypertension

4. Awareness,treatment and control of hypertension in HIV positive patients.

Table 3. Studies identifying factors associated with hypertension among HIV-positive populations

Study	Country	Study design (duration in years)	Sample size; % men	Mean age (years)	Association				
					HIV duration	CD4 count	Viral load	ART	ART duration
Americas									
Khalsa, et al. (2007)[23]	USA	Cohort (5)	2,059 women	–	–	No	No	No	No
Crane, et al. (2006)[49]	USA	Cohort (7)	444; 84%	35	–	(≥ 200 cells/μl Negative	No	Yes	No
Seaberg, et al. (2005)[51]	USA	Cohort (20)	5,578 men	32.6	No	–	–	–	ART ≥ 2 yrs Positive
Medina-Torne, et al. (2012)[15]	USA	Cross-sectional	707; 92% male	41	(≥ 10 yrs) Positive	No	Negative	No	No
Krauskopf, et al. (2013)[14]	USA	Cross-sectional	2,390	43	(≥ 6 yrs) Positive	Positive	No	No	–
	USA	Prospective cohort	2,390	43	No	No	No	No	–
Factor, et al. (2013)[43]	USA	Cohort (3)	329 men	54.4	–	No	–	Negative	–
	USA	Cohort (3)	330 women	43.4	–	Positive	–	No	–
Miguez-Burbano, et al. (2014)[47]	USA	Cohort (not provided)	400	42	No	No	No	No	No
de Arruda, et al. (2010)[44]	Brazil	Case-control	958	–	–	No	–	No	No
Europe									
Palacios, et al. (2006)[50]	Spain	Cohort (1)	95	40	–	Negative	–	–	Positive
Coloma Conde, et al. (2008)[27]	Spain	Retrospective	740; 75% male	41.8	No	No	No	–	No
Bernardino, et al. (2011)[46]	Spain	Cross-sectional	310; 76.8% male	42	(≥ 10 yrs) No	No	No	Positive	No
Bakken, et al. (2008)[26]	Norway	Cohort	542	–	No	–	–	–	HAART ≥ 5 yrs Positive
Manner, et al. (2012)[28]	Norway	Cohort (3)	434	43	(≥ 10 yrs) Positive	No	No	No	No
Jung, et al. (2004)[45]	Germany	Cohort (1)	214	42	(7 yrs) No	No	No	No	No

Asia									
Hejazi, et al. (2013)[45]	Malaysia	Cross-sectional	340	–	(≥ 10 yrs) No	No	No	No	No
Africa									
Diouf, et al. (2012)[19]	Senegal	Cross-sectional	242	46	–	No	No	–	No
Denue, et al. (2012)[18]	Nigeria	Cohort (2)	227	40	No	No	–	–	HAART ≥ 2 yrs Positive
Ogunmol, et al. (2014)[21]	Nigeria	Cross-sectional	403	–	–	No	–	No	No
Bloomfield, et al. (2013)[17]	Kenya	Retrospective (3)	12,194; 35.2%	–	–	Positive in women	–	–	No
Peck, et al. (2014)[22]	Tanzania	Cross-sectional	454	–	–	(> 500) Positive	–	Positive	No
Dillon, et al. (2013)[61]	14 countries	Meta-analysis of 52 cross-sectional studies	29,755	–	–	–	–	Positive	–

Among the twelve studies which assessed the relationship between duration of HIV infection and presence of hypertension ,two studies reported positive associations which were statistically significant.The association was found to be more in patients who had HIV for more than 10 years,independent of HAART use or age,indicating that a shorter exposure period may not be enough to demonstrate association with HIV and hypertension.(40)

In a study conducted in Poland, 28% of HIV patients were found to have hypertension and there was increased prevalence in all age ranges: < 40, between 41-60 and > 60 which were 18%, 43% and 53% respectively. Among the hypertensives, grade I, II and III hypertension was observed in 58%, 35% and 7% of patients, respectively.

Risk factors found were:

1. increasing age

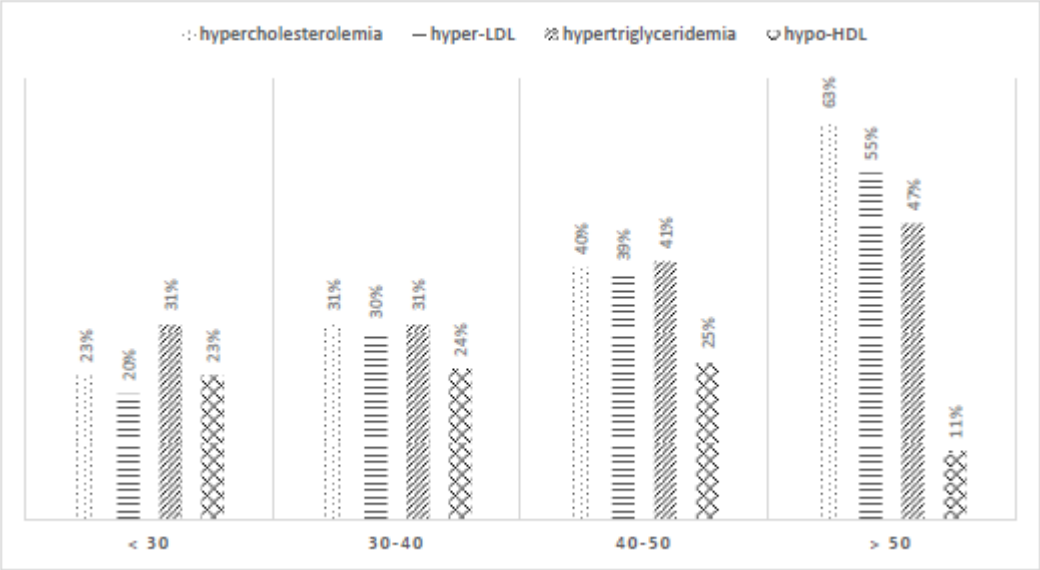
2. male sex
3. increased BMI
4. hypercholesterolemia
5. low HDL
6. hypertriglyceridemia
7. duration of HIV infection greater than 10 years (41)

4.5 DYSLIPIDEMIA

In the same study mentioned above,which included 417 HIV infected Caucasian adults, hypercholesterolemia was observed in 37% of the study group, suboptimal level of HDL in 20.5% and increased LDL in 31% of patients. Hypertriglyceridemia was detected in 52% of patients, of which it was more than 150mg/dL in 35%. Mixed hyperlipidaemia (concurrent elevated LDL and TG levels) was diagnosed in 21% of patients. Lipids concentrations were similar for both sexes , excluding optimal triglyceride level, which was more often observed in females than males (55% vs 45%, p=0.05).

Patients on HAART when compared with those not on HAART had higher

levels of total cholesterol (mean 178, IQR 153.5-212.5, p=0.0005) and triglycerides (mean 121, IQR 85-189, p=0.001).(41)



Elevated triglyceride levels (OR: 2,83; 95% CI:1,04 – 7,71) was the only lipid abnormality associated with HAART and further analysis it was associated with protease inhibitor based treatment (OR: 2.56;95% CI: 1,66 – 3,96). There was statistically significant association between cigarette smoking and hypercholesterolemia (p=0,03),hypertriglyceridemia (p=0,01) and mixed hyperlipidaemia (p=0,04).

The prevalence of metabolic complications in all HIV-infected patients in the Korea HIV/AIDS cohort study was as follows. The prevalence of obesity based on BMI was 16.4%, obesity based on waist/hip ratio was 19%, that of hyperglycemia was 10.4%, hypercholesterolemia 6%, elevated LDL levels 5.5%, and hypertriglyceridemia 32.1%

respectively. Among metabolic parameters, median serum total cholesterol (155 [48–297] vs. 176 [11–364] mg/dL; $P < 0.001$), HDL-cholesterol (38 [4–137] vs. 45 [10–177] mg/dL; $P < 0.001$), and triglycerides (155 [14–636] vs. 202 [18–1,040] mg/dL; $P < 0.001$) were significantly higher in treatment-experienced patients . Also, both hypercholesterolemia (2.7% vs. 7.7%; $P = 0.008$) and hypertriglyceridemia (23.7% vs. 37.2%; $P < 0.001$) showed a statistically significant higher value in patients who received HAART compared with those who did not.(42)

In a study conducted in Congo,it was found that 11.9% of HIV infected patients had a total cholesterol greater than 200 mg/dl versus 7.4% of HIV negative individuals (P=0.019). For HDL-cholesterol, 36.40% of HIV-infected patients had a serum fasting ≤ 40 mg/dl versus 15.70% of HIV negative individuals (P < 0.001). Median fasting total cholesterol was also elevated (140 mg/ dl) in HIV positive patients when compared to those who were not/ (133mg/dl) [P=0.015].HIV uninfected patients had a median fasting HDL-cholesterol higher (58.5 mg/dl) than HIV-infected patients (49 mg/dl) [P < 0.001]. HIV-infected women were more likely to have a higher mean of total cholesterol: 147.70 ± 52.09 mg/dl versus 135.72 ± 48.23 mg/dl for the HIV-infected men (P = 0.014) and of HDL-cholesterol: 55.80 ± 30.77 mg/dl as compared to 48.24 ± 28.57mg/dl for the HIV-infected men (P = 0.008). Being HIV positive on first-line antiretroviral therapy based on stavudine-lamivudine-nevirapine was associated with high prevalence of total cholesterol > 200 mg/dl and HDL-cholesterol ≤ 40 mg/dl. (43)

In another study conducted in Cameroon it was found that receiving HAART and HIV duration of 42 months and more were independently associated with total cholesterol ≥ 200 mg/dL. Receiving HAART was independently associated with raised LDL-cholesterol values.(44)

A Brazilian study showed low HDL as the most frequent abnormality (53.7% of patients had levels < 40 mg/dL), followed by elevated triglyceride levels (36.1% of patients had levels > 200 mg/dL) among a sample of 93 HIV patients who were on ART from 2005 to 2006.(45)

4.6 ISCHAEMIC HEART DISEASE AND STROKE

The presence of diabetes,hypertension and dyslipidemia invariably contributes to the development of vascular diseases.

Although the incidence of cardiovascular diseases classically associated with human immunodeficiency virus has decreased considerably with antiretroviral therapy, cardiovascular risk, and especially ischemic heart disease, are higher in HIV-infected patients than in uninfected individuals. This is due to the interaction of patient-dependent factors with virus-dependent factors, as well as factors associated with antiretroviral therapy. With increasing of life expectancy and the chronicity of HIV infection, cardiovascular disease has emerged as an important cause of morbidity and mortality in HIV patients.

The largest prospective study of cardiovascular risk with ART is the Data Collection on Adverse Events of Anti-HIV Drugs (DAD) study.Of 23 437 participants, 345 (1.5%) developed a first MI, an incidence of 3.7 per 1000 person-years. Of these, 29% were fatal, representing 10% of all deaths in the study.

Incidence of MI increased directly with longer exposure to ART (relative risk 1.16, 95% CI 1.09 to 1.23, per year of exposure, $P<0.0001$) for up to 6 to 7 years of exposure.

Importantly, this relative association between exposure to ART and increased risk of MI was comparable irrespective of age or gender.

In further analyses evaluating the impact of individual antiretroviral drug classes, the relative risk of protease inhibitor therapy was also 1.16 (95% CI 1.10 to 1.23, $P<0.001$) whereas the annual relative risk for non nucleoside reverse-transcriptase inhibitor–based therapy was not significant (relative risk 1.05, 95% CI 0.98 to 1.13).(46)

A recent large cohort study found a strong and consistent association of HIV with a 50% increased risk of MI, independent of traditional risk factors, such as age, race, socioeconomic status, and substance abuse .(47)

Table 2. Rates of AMI by HIV Status and Age Group[a]

Status	Age Group, y							
	<30	30-39	40-49	50-59	60-69	70-79	80-89	>89
Uninfected								
No. of participants	1175	6783	21 866	19 805	4209	1120	148	3
No. of AMI events	0	10	164	218	66	36	14	0
AMI rates per 1000 person-years (95% CI)	...	0.3 (0.2-0.6)	1.5 (1.3-1.7)	2.2 (1.9-2.5)	3.3 (2.6-4.2)	6.7 (4.8-9.2)	21.5 (12.7-36.4)	...
HIV Infected								
No. of participants	725	3848	10 575	9342	2065	557	56	0
No. of AMI events	0	13	105	171	46	25	3	0
AMI rates per 1000 person-years (95% CI)	...	0.7 (0.4-1.2)	2.0 (1.6-2.4)	3.9 (3.3-4.5)	5.0 (3.8-6.7)	10.0 (6.7-14.7)	13.5 (4.3-42.0)	...
Incidence rate ratio (95% CI)	...	2.19 (0.89-5.58)	1.34 (1.04-1.72)	1.80 (1.47-1.21)	1.53 (1.03-2.26)	1.50 (0.86-2.57)	0.63 (0.12-2.25)	...

The findings of the SMART (Strategies for Management of Antiretroviral Therapy) trial also suggest that HIV and attendant inflammation are important in conferring risk for ischaemic heart disease. (48)

This is further supported by a recent study, which found that new cycles of HIV replication may also play a role in ongoing inflammation in patients with modest antiretroviral therapy nonadherence . In HIV-infected patients, studies suggest that immunodeficiency (CD4+ cell counts <200 cells/mm^3) is significantly associated with a higher risk of MI.(49)

4.7 CHRONIC KIDNEY DISEASE

Even though exact epidemiologic data are missing because of the use of different screening techniques, chronic kidney disease in HIV-infected patients is a common and clinically relevant finding.

Proteinuria and elevated creatinine level have been found in 7.2%(50) to 32% (51) of HIV-seropositive patients and were associated with an increased rate of death in a study of 2038 female HIV-infected patients in a study conducted in Durham.(52)

HAART has been found to reduce progression from AIDS to end- stage renal disease in patients of African descent by 38%, yet a significant increase in the prevalence of end-stage renal disease (ESRD) associated with an increase in the prevalence of HIV infection in this population has been predicted.(53)

In a cohort study conducted in Western India to assess nephrotoxicity of Tenofovir, it was found that of 1,271 patients started on a Tenofovir containing antiretroviral treatment (ART) 83 (6.53%) developed renal dysfunction, of which 79 had impaired serum creatinine and five had Fanconi's syndrome. Renal dysfunction was more common with boosted a protease inhibitor (PI) (9.44%) based regimen as compared to a non nucleoside reverse transcriptase inhibitors (NNRTI) (5.01%)-based regimen ($P = 0.003$). The mean decline in creatinine clearance from baseline was 22.27 ml/min.(54)

Recently, the EuroSIDA study reported that only 0.64% of 9044 patients developed advanced CKD/ESRD/renal death during a median follow-up of 5.0 years, with an incidence rate of 1.32 per 1000 personyears follow-up. At 6 years from baseline, 0.83% were estimated to have experienced the endpoint overall.(55)

Traditional risk factors for CKD are becoming increasingly prevalent in HIV-infected populations, including aging, diabetes mellitus, hypertension, cardiovascular disease, previous AKI and race/ethnicity (56).

Risk factors for CKD in HIV-persons are therefore a combination of traditional and HIV-related factors including low CD4 counts, high viral load, intravenous drug use, HCV co-infection and also cART, mainly tenofovir, indinavir, lopinavir/ritonavir, atazanavir/ritonavir and abacavir.(57)

4.8 OSTEOPOROSIS

Randomized controlled trials comparing bone mineral density in protease inhibitor (PI) vs non-PI regimens have shown mixed results, with some studies revealing that PI-containing regimens led to decreased spine BMD and others showing no difference in total body or hip BMD between treatment groups.(58) (59)

Randomized trials comparing BMD in tenofovir and non tenofovir regimens have consistently found that tenofovir is associated with significantly decreased BMD at the hip and spine.(60,61)

During the HAART era, cumulative exposure to tenofovir was associated with an increased risk of incident fracture (HR, 1.16; 95% CI, 1.08–1.24; $P < .0001$)(62)

Similar to general population, osteoporosis is an important risk factor for fracture among HIV patients . Among 1006 participants in a cohort study, the presence of osteoporosis was associated with a fourfold increased risk of incident fracture (mainly of the rib or sternum, hand, foot, and wrist). Prevention of osteoporotic fractures is of utmost importance in this population as the longevity is also currently being increased as compared to olden times.(63)

Another study in Italy showed that lower femoral Z-score was independently associated with factors like low BMI, AIDS diagnosis, HCV co-infection, antiretroviral treatment, and non traumatic bone fractures; a lower lumbar Z-score was associated with age, BMI, CD4 T-cell counts, and non traumatic bone fractures. Prevalence of non traumatic bone fractures was 27.0%, predictors being male gender, HCV co-infection, and lower femoral Z-scores. The results of this study suggest that measuring bone mineral density by DEXA in all HIV patients regardless of any further specification may help retrieving one-fifth of patients with early osteoporosis not identified using current criteria for selective screening of bone mineral density(64).

A study conducted in Taiwan revealed that mong 320 patients with a median age of 37.3 years, body mass index (BMI) of 21.4 and 94.4% on ART, osteopenia and osteoporosis were diagnosed in 35.6% and 3.8%, respectively. On multivariate linear analysis, factors associated with reduced BMD were increasing age (p=0.006), longer duration on antiretroviral therapy (p=0.007), and a decreasing BMI (p=0.002). Being underweight with a body mass index

(BMI) less than 18.5 was independently associated with reduced BMD (proportional odds ratio, 4.12; 95% confidence interval, 1.93-8.82).(65)

4.9 LIPODYSTROPHY

Lipodystrophy can be either lipoatrophy or lipohypertrophy,both of which can be found in individuals taking long term HAART.

Exposure to NRTIs-

Data suggest that exposure to certain NRTIs is the major factor associated with lipoatrophy . Trials comparing different antiviral regimens suggest that thymidine analogs (in particular stavudine, but also zidovudine) play an important role in pathogenesis of lipoatrophy.(66)

Prevalence of lipoatrophy was found to be increased with the use of stavudine and indinavir, and lipoaccumulation was associated with duration of ART in a study conducted among 1077 patients visiting HIV Out Patient Study Clinics.(67)

In a subset of patients participating in an open-label randomized trial comparing tenofovir-emtricitabine and zidovudine-lamivudine, each in combination with efavirenz, total limb fat, as measured by dual energy x-ray absorptiometry (DEXA), was less with zidovudine than tenofovir (mean 6.9 versus 8.0 kg fat)(68)

Exposure to other ART classes-

Some studies have suggested that although NRTI use contributes to fat wasting, protease inhibitors may act synergistically with NRTIs .(69) However, therapy with protease inhibitors alone does not appear to lead to lipoatrophy .

Similarly, in a metabolic substudy of a trial evaluating various ART regimens (ACTG 5142), the incidence of lipodystrophy was higher with efavirenz plus two NRTIs compared with lopinavir plus two NRTIs or efavirenz plus lopinavir, but the association between efavirenz and lipoatrophy was mainly in combination with stavudine or lamivudine, not tenofovir.(70)

4.10 QUALITY OF LIFE ASSESSMENT

HIV is a disease which not only affects a person physically.but also socially and psychologically.Hence evaluation of quality of life becomes important in these patients.

A study conducted in Orissa to evaluate the same in a group of 153 patients on antiretroviral therapy found that the overall QOL score was moderate(using the WHOQOL HIV BREF questionnaire).Also lower BMIs were associated with poorer QOL scores.(71)

Another study done in a tertiary care centre in South India using the same questionnaire showed that the overall mean score for quality of life in a scale of 0 to 20 was 13.29,lowest individual score being in the social relationship domain. (72)

A study conducted in Xinjiang province in China showed alarming findings of high stigmatization: 86% of the patients were afraid to tell others they were HIV positive and 69% often felt or always felt depressed. Only 1% of the patients were on antidepressant treatment.(73)

An Australian study conducted detailed interviews which revealed the long standing difficulties of living with HIV,particularly in the domains of intimate relationships, perceived stigma, and chronic ill health.

The factors related to lower health related quality of life(HRQL) were:

1. newly diagnosed HIV ($p=0.001$)

2. never received anti-retroviral treatment ($p=0.009$);

3. depression, unemployment or a high frequency of adverse symptoms, (all $p<0.001$).

Total quality of life was reduced by perceived stigma with 33% of surveyed patients reporting persistent fears of both disclosing their HIV status and infecting others.

The analysis showed that psychological distress had a large impact on quality of life in this cohort. This was accentuated in people with poor physical health which in turn was associated with unemployment and depression. People with HIV infection are living longer and residual side effects of the earlier regimens complicate current clinical management and affect their quality of life. However, even for the newly diagnosed exposed to less toxic regimens, HIV-related stigma plays an important role in building negative social and psychological effects. Context-specific interventions are required to address persistent distress related to stigma, reframe personal and public perceptions of HIV infection and alleviate its disabling social and psychological effects.(74)

4.11 LACUNAE IN CURRENT KNOWLEDGE AND JUSTIFICATION

Thus there is a need to look at the individual chronic disease profile of HIV patients who have been on long term antiretroviral therapy in our hospital and thereby assess their cardiovascular risk and adequacy of treatment .The duration of ART in all of the previous Indian studies has been less than 5 years.Here we aim to look at the chronic diease profile with respect to a longer duration of ART of more than or equal to 5 years.Moreover,the adequacy of treatment of these diseases has not been looked at in earlier studies.It will also be useful to look at their quality of life so that we can modify our standard of care to improve the same as well.

5.MATERIALS AND METHODS

5.1 STUDY SETTING

The study was conducted in Christian Medical College, Vellore (CMC), a tertiary care level hospital situated in Vellore, Tamil Nadu. Patients were recruited from those attending the General Medicine OPD of CMC Vellore.

5.2 STUDY DESIGN

This is a cross sectional study to evaluate the presence of chronic diseases among HIV patients on antiretroviral therapy for more than or equal to 5 years.

HIV positive patients presenting to the out patient department of General Medicine Unit 1 were recruited as per inclusion and exclusion criteria given below.

Diagnostic criteria for chronic diseases included in the study are as described in appendix.

5.3 PARTICIPANTS

INCLUSION CRITERIA

All patients detected to be HIV positive in our hospital and who have received ART for more than or equal to 5 years and on follow up with Medicine 1 OPD.

EXCLUSION CRITERIA

Age less than 18 years.

Patients who have developed any of the chronic diseases of interest prior to initiation of ART.

5.4 SAMPLE SIZE

As our study aims at assessment of chronic disease profile of HIV patients on long term antiretroviral therapy,and not prevalence or incidence of any of the diseases per se,sample size calculation based on previous studies was not feasible.Hence it was decided to include in the study, all patients satisfying the inclusion criteria who were registered with Medicine 1 OPD and who have been on ART for more than or equal to 5 years.The estimated number of such patients satisfying the inclusion criteria which was obtained based on chart review is 50.Sample collection was started after Institutional Review Board approval of the same.

5.5 METHOD OF RECRUITMENT

Institutional Review Board approval and Ethics Committee approval was obtained (IRB Min No 10024, dated 04/04/2016).

After the approval, patients presenting to the Department of General Medicine, who met the inclusion criteria were enrolled in the study via convenient sampling.

5.6 FUNDING

The protocol was approved by the Institutional Review Board and funding was provided by the FLUID research grant of IRB.

5.7 METHOD OF EVALUATION

HIV positive patients presenting to the out patient department of General Medicine Unit 1 OPD were recruited as per inclusion and exclusion criteria.

The following were undertaken.

1) **Informed written consent** were taken from all participants by the principal investigator. The consent as taken after giving written information regarding nature of the study, verbal explanation of the same and clarification of the queries.

2) A **questionnaire** including demographic details of all study participants, treatment details,smoking history, history of alcohol consumption, was administered by the principal investigator.

3) **Quality of life assessment** was done using WHOQOL BREF Questionnaire.

4) **Physical examination** including systolic and diastolic blood pressure, height and weight,waist circumference was done by the principal investigator.

5) **Blood pressure** was taken with a standardized sphygmomanometer. Readings were taken with the patient seated on a chair for 15 minutes of rest. Blood pressure reading in mm Hg was taken in the right upper limb.

6) **Height** was measured using a stadiometer to the nearest 0.1cm.

7) **Weight** was measured using a calibrated weighing machine to the nearest 0.1kg. . BMI will be calculated.

8) **Waist circumference** was measured using a stretch resistant tape at the mid- point between lower margin of last palpable rib and top of iliac crest to the nearest 0.1cm. Measurement was taken at the end of normal expiration, with the subject relaxed, standing with feet close to each other and arms by side.

5.8 VARIABLES

Demographic:Age,Sex,Occupation,Level of education,Native state

Presence of:

1) Diabetes mellitus

2) Hypertension

3) Dyslipidemia

4) Ischemic heart disease

5) Cerebrovascular disease

6) Chronic kidney disease

7) Osteoporosis

8) Lipodystrophy

9)Date of ART initiation

10) Details of ART drugs

11) Smoking status,smoking pack years and number of years since quitting smoking if reformed smoker

12)Drinking status,duration and frequency of alcohol intake and quantity of alcohol consumed per day.

Clinical Examination:

13)Blood pressure

14)Height

15)Weight

16)Body mass index

17)Waist circumference

The following tests were done(if not already been done) in addition to history and clinical examination to evaluate for the above mentioned conditions.

Fasting and 2 hours post prandial blood sugar

HbA1c

Total cholesterol,HDl,LDL and Triglycrides(Fasting)

Serum creatinine and blood urea

ECG,Treadmill test (in patients who are symptomatic or have ECG changes)

DEXA scan-for bone mineral density to define osteoporosis as well as whole body fat analysis to define lipodystrophy.

Trunk fat/lower limb fat mass ratio >2.28 identified 54.3% of patients with HIV receiving HAART as having lipodystrophy and had the highest odds ratio for predicting metabolic syndrome; based on a previous study conducted in our institution which developed an

objective definition of HIV associated lipodystrophy using regional fat mass ratios.(75) Hence we used trunk fat/lower limb fat mass ratio more than 2.28 as cut off for defining lipodystrophy. DEXA for the same was done along with the whole body DEXA which was done for assessment of bone mineral density.

The above mentioned chronic diseases are defined as per standard criteria described in annexure.

The presence of each of the diseases were assessed as well as adequacy of treatment of diabetes,hypertension and dyslipidemia were assessed based on standard criteria for treatment goals as described in annexure.

For adequacy of control of diabetes, 3 different values of HbA1c were taken at different points of time and the average was calculated to assess the adequacy of treatment.If the average Hba1c was less than or equal to 7,it was considered as adequate control and if more than 7,it was considered not well controlled.

For adequacy of control of hypertension, 3 different values of blood pressure recordings were taken at different points of time and the average was calculated to assess the adequacy of treatment.If the average blood pressure was less than 140/90mmhg, it was considered as adequate control and if more than or equal to 140/90mmhg, it was considered not well controlled.

For adequacy of control of dyslipidemia, 3 different values of LDL values were taken at different points of time and the average was calculated to assess the adequacy of treatment.If the average LDL was less than 100mg/dL it was considered as adequate control and if more than or equal to 100mg/dL , it was considered not well controlled.

Quality of life was assessed based on WHOQOL HIV BREF questionnaire. It was calculated using the WHO QOL HIV BREF scale which has six domain scores namely physical, psychological, level of independence, social relationships, environmental, and spirituality, religion, personal beliefs (SRPB).

Individual items are rated on a 5-point Likert scale where 1 indicates low, negative perceptions and 5 indicates high, positive perceptions.

Higher score indicates better QOL. For better result interpretations, the QOL scores between 4 - 9.9 were taken as low scores, 10 -14.9 as medium scores, and 15 - 20 as high score.(71)

Scores were calculated using SPSS software version 17.

Cardiovascular risk was calculated based on American Heart Association Guidelines 2013 Risk Calculator.

5.9 STATISTICAL ANALYSIS

Data from the clinical research form were entered into the Epidata v 3.1 data entry software and then exported to SPSS version 17, IBM Corporation for analysis. All analysis was performed by trained biostatistician Mrs Mahasampath Gowri.

For continuous data , the descriptive statistics Mean, Standard deviation, Median, Minimum and Maximum are presented. For categorical data, the number of patients and percentage are presented. Based on the normality of data, the parametric t test or nonparametric Mann - Whitney test were applied to the data. The Chi-square or Fisher exact test was applied to the data when required.

P value less than 0.05 was considered statistically significant.

There were mainly 4 different ART drug groups namely :

T E E/T L E-Tenofovir+Emtricitabine+Efavirenz/Tenofovir+Lamivudine+Efavirenz

Z L N-Zidovudine+Lamivudine+Nevirapine

S L N –Stavudine+Lamivudine+ Nevirapine

T E At Rt- Tenofovir+Emtricitabine+Atazanavir+Ritonavir

For statistical analysis,TEE and TLE were grouped into one group and ZLN and SLN were grouped into one group for comparison.T E At Rt could not be included in P value calculation using chi square test in view of very small number of patients (less than 5) included in the group.

6. RESULTS

The study was conducted from 1st June 2016 to 1st June 2017.

50 patients were recruited in the study as per inclusion criteria.

6.1 DEMOGRAPHIC VARIABLES

AGE

The mean age was 48.46± 8.77,the least being 20 years and the highest being 65 years.

GENDER

Males were more in number and constituted 38 out of 50,that is 76% of the total number .

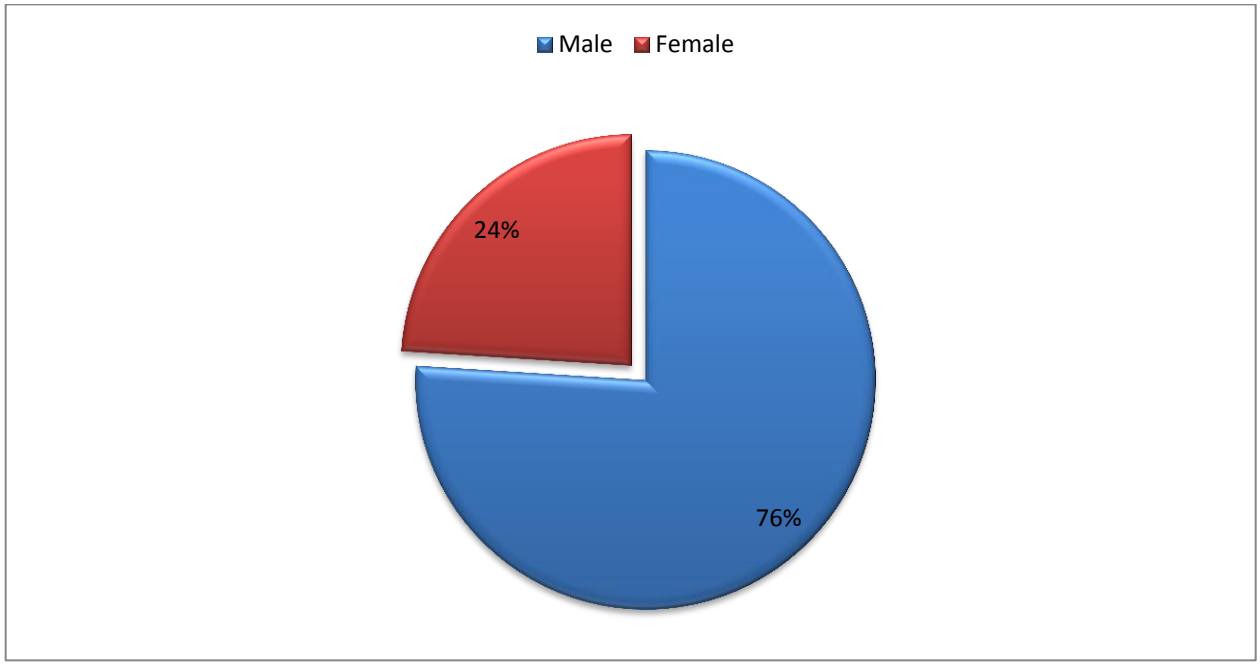


Figure 1-Gender distribution

NATIVE STATE

Majority of patients were from Tamil Nadu,22 out of 50 (44%) and Andhra Pradesh 20 out of 50(40%).2% each were from Kerala and Jharkhand. 4% each were from Pondicherry, Bihar and Manipur.

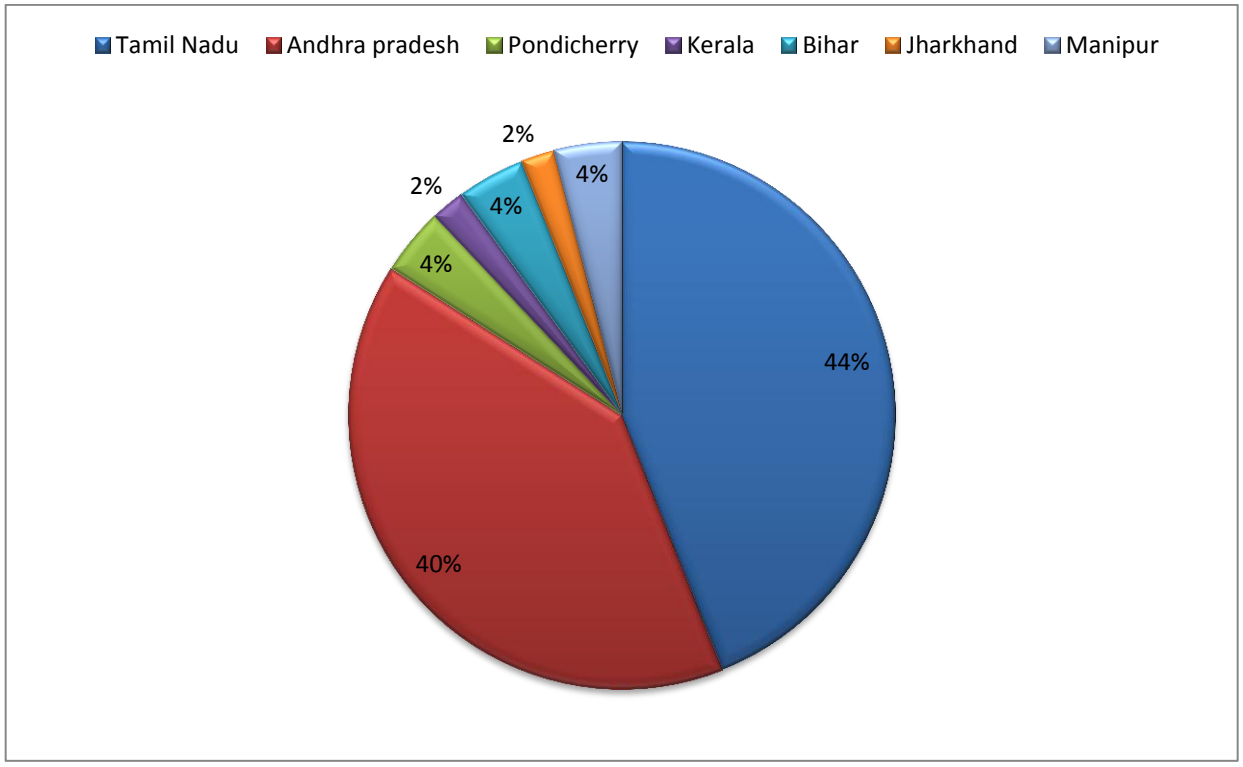


Figure 2-Place distribution according to native state

LEVEL OF EDUCATION

Educational qualification wise, most patients belonged to high school and

intermediate or diploma groups.36% constituted intermediate or diploma qualification while 20% constituted high school qualification.

The percentages of primary school and middle school qualification were 8% and 16% respectively.Another 16% had graduate or postgraduate degree, while 4 % had professional qualifications.

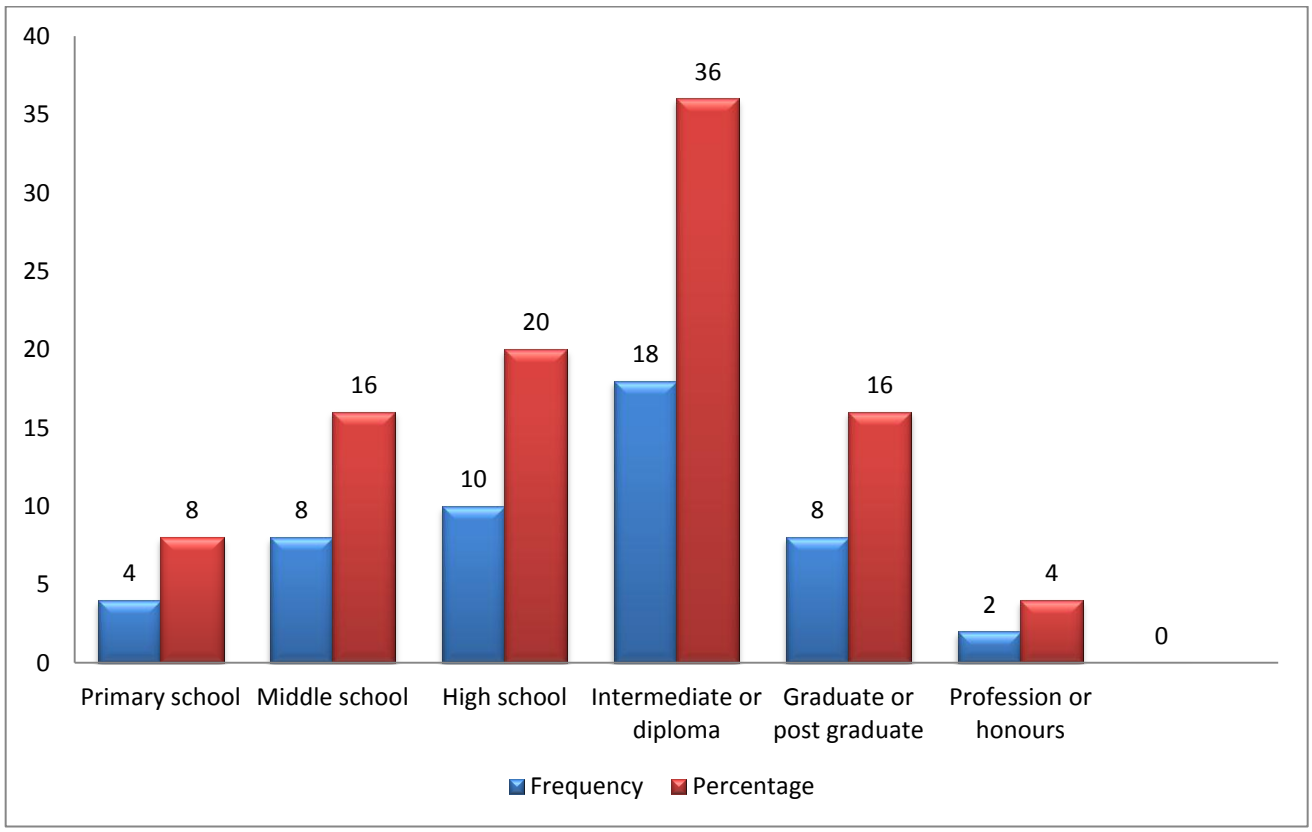


Figure 3-Level of education of study population

OCCUPATION

The distribution of occupation among the patients reflected most patients being in the semi professional group,that is 22 % of the total study population.12% were unemployed,10% belonged to unskilled group,14% were semiskilled,18% each were either skilled or belonged to clerical,shop owner or farmer group.6% had professional jobs.

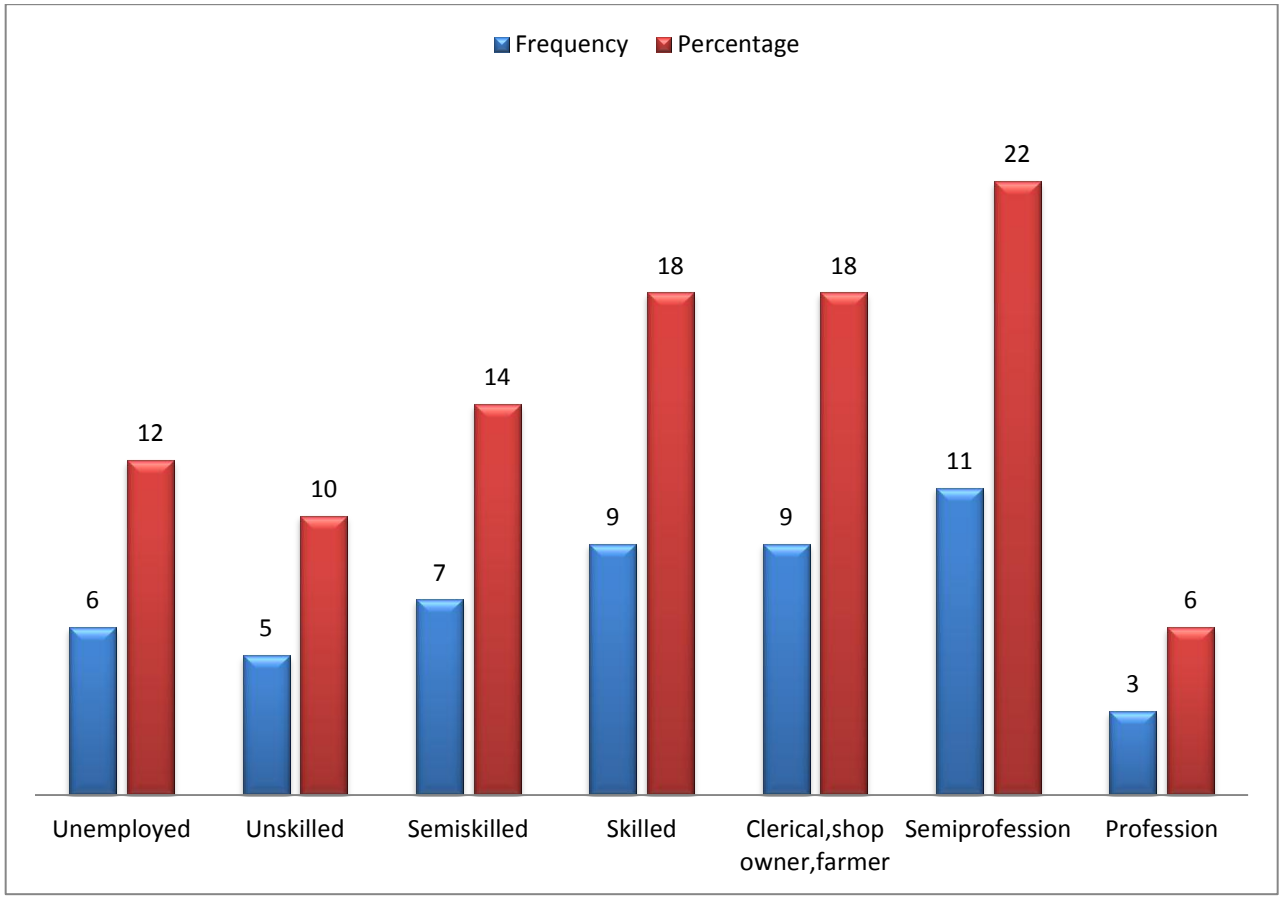


Figure 4-Distribution of occupation among study population.

6.2 ART DRUG GROUPS

The four main groups of ART drugs into which patients were categorised according to drug regimen are as follows:

T E E/T L E-Tenofovir+Emtricitabine+Efavirenz/Tenofovir+Lamivudine+Efavirenz

Z L N-Zidovudine+Lamivudine+Nevirapine

S L N –Stavudine+Lamivudine+ Nevirapine

T E At Rt- Tenofovir+Emtricitabine+Atazanavir+Ritonavir

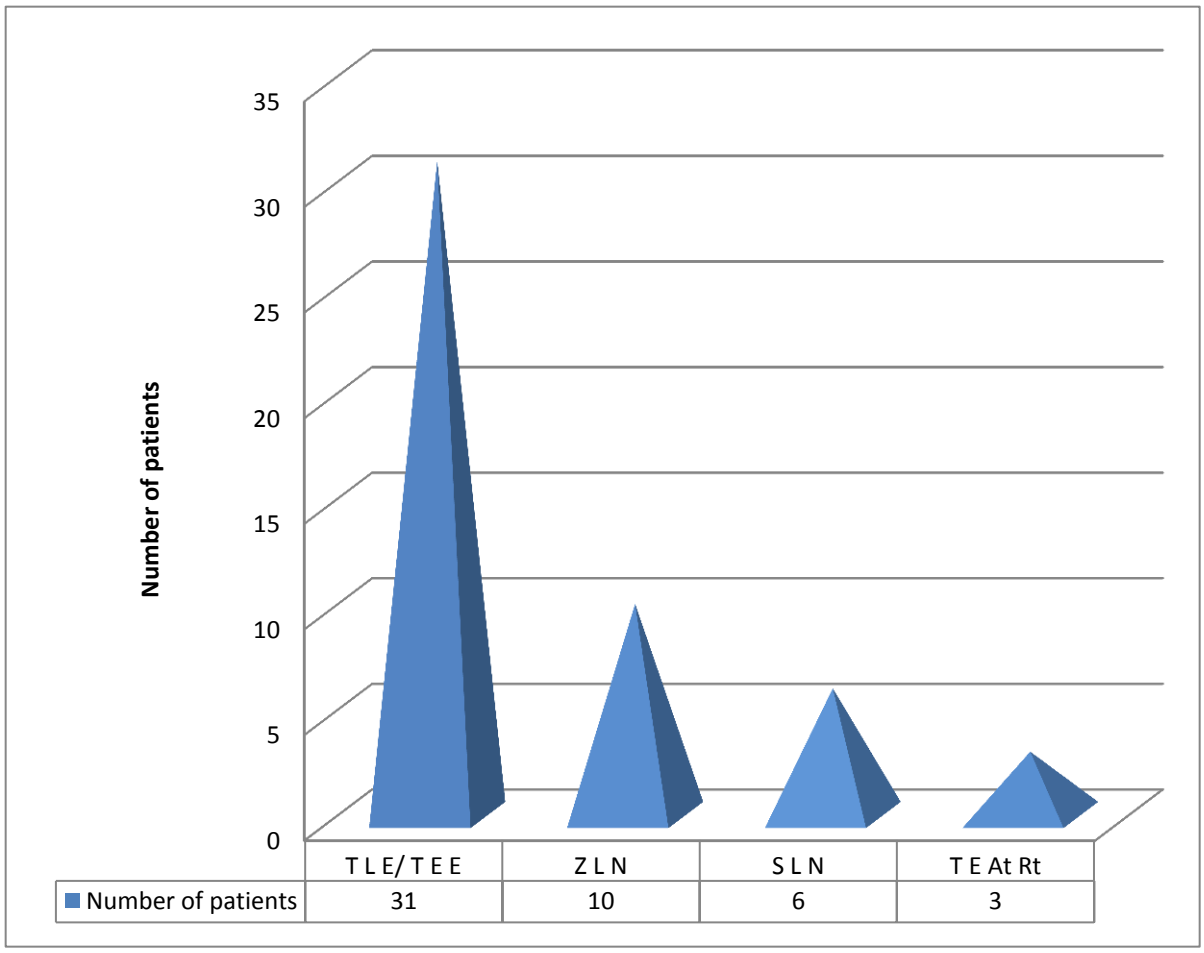


Figure 5-ART drug groups

6.3 CHRONIC DISEASE PROFILE OF STUDY POPULATION

Assessment of chronic disease profile of the recruited sample of patients led to the following results**:**

DIABETES MELLITUS

20 among the 50 recruited patients were found to have diabetes based on standard guidelines,which constitute 40% of total patients.

All patients with diabetes were above the age of 40 years.

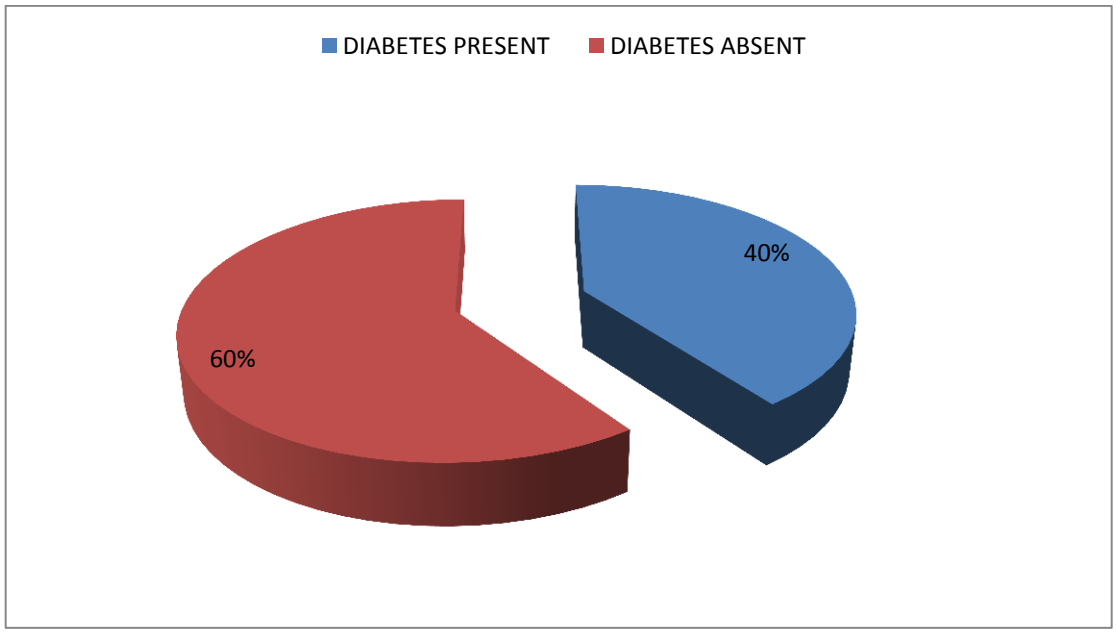


Figure 6-Distribution of diabetes among study population

Comparison of the different ART drug groups with diabetes is shown in Figure 6.

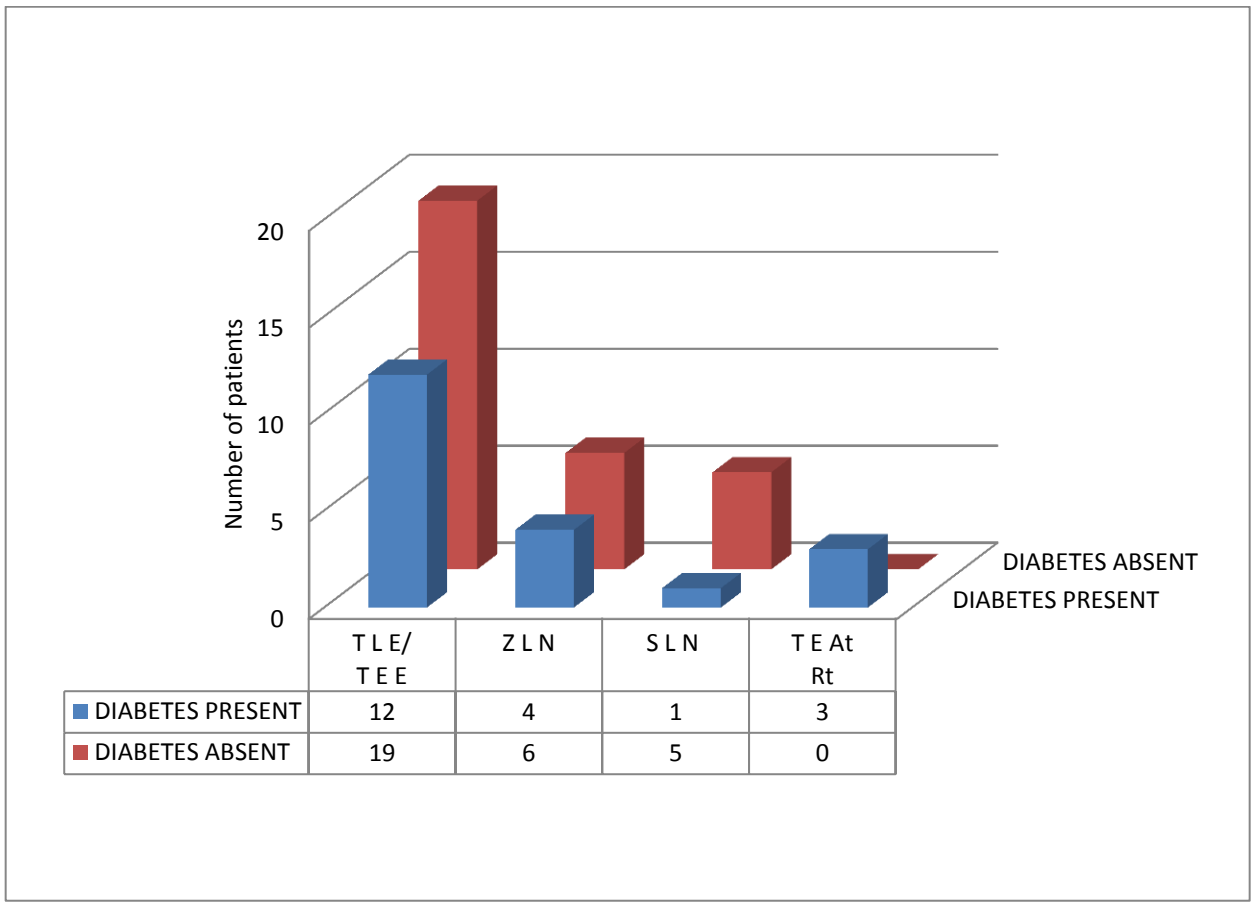


Figure 7-Comparison of ART group with diabetes

12 out of 31 patients in the TEE/TLE group were found to have diabetes, as compared to 4 out of 10 in ZLN group and 1 out of 6 in SLN group. Only 3 patients were on Tenofovir Emtricitabine Atazanavir Ritonavir and all 3 of them were confirmed to have diabetes.

Table 1-Comparison of ART group with diabetes

Diabetes	TEE/TLE	ZLN/SLN	T E At Rt	Total
Yes	12(38.71%)	5(31.25%)	3(100%)	20 (40%)
No	19(61.29%)	11(68.75%)	0(0%)	30(60%)
Total	31(100%)	16(100%)	3(100%)	50(100%)

Pearson chi 2=0.2544 P=0.614

There was no statistically significant association between type of ART drug and diabetes in the study population.

Table 2-Duration of ART versus diabetes

Diabetes	Number of patients	Mean duration of ART	95% confidence interval
Yes	20	9.241±3.34	(7.6802-10.8019)
No	30	9.538±2.87	(8.4660-10.6118)

P value=0.7378

Using two sample T test with equal variances, P value of 0.7378 was computed and the mean duration of ART was found to be not statistically different in groups who developed diabetes and those who did not.

HYPERTENSION

Only 13 patients were found to have hypertension among the 50,which constitute 26% of total patients.

All patients with hypertension were above the age of 40 years.

Comparison of ART drug groups with hypertension is shown in Figure 7.

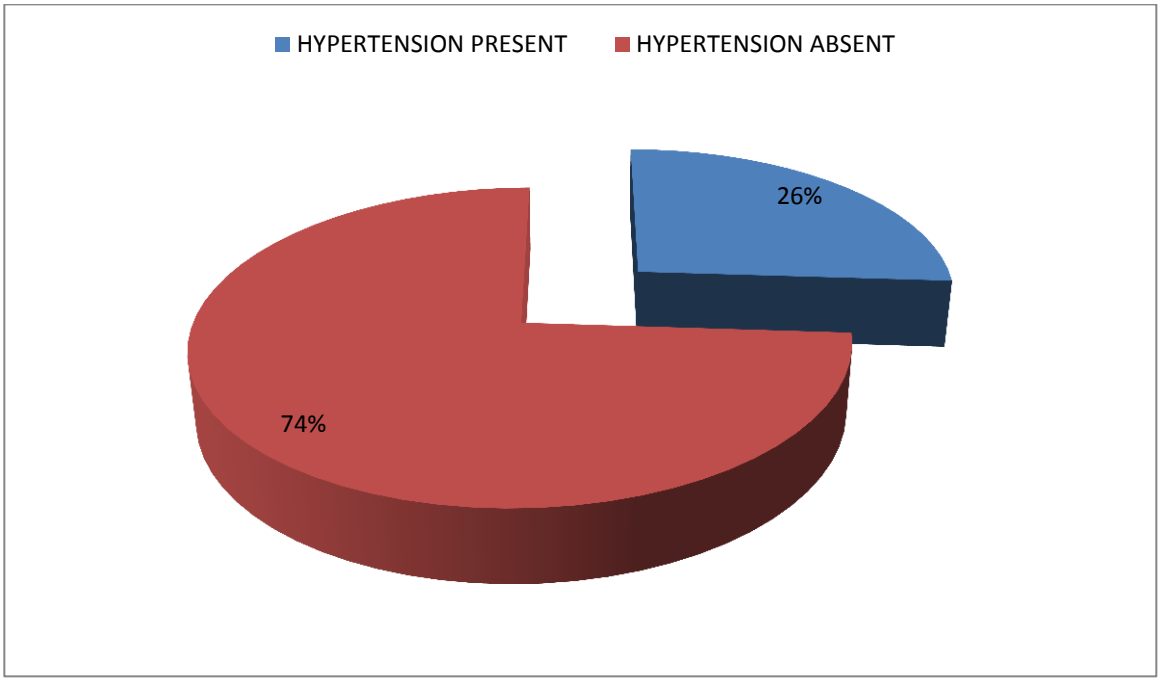


Figure 8-Distribution of hypertension among study population

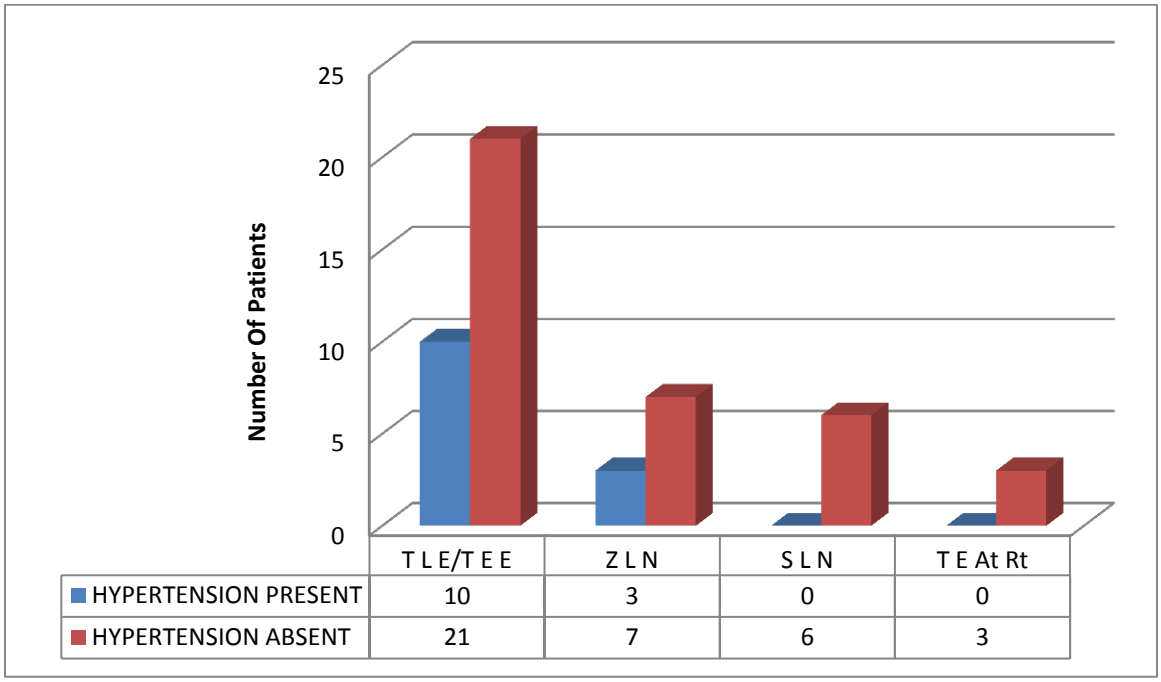


Figure 9-Comparison of ART drug group with hypertension

Hypertension was found in 10 out of 31 patients in the TEE/TLE group and 3 out of 7 in the ZLN group.Neither SLN nor TE At Rt groups had patients with hypertension.

Table 3-Comparison of ART drug group with hypertension

Hypertension	TEE/TLE	ZLN/SLN	T E At Rt	Total
Yes	10(32.26%)	3(18.75%)	0(0%)	13(26%)
No	21(67.74%)	13(81.25%)	3(100%)	37(74%)

Total	31(100%)	16(100%)	3(100%)	50(100%)

Pearson chi 2=0.9624 P=0.327

There was no statistically significant association between type of ART drug and hypertension among the recruited sample of patients.

Table 4-Duration of ART versus hypertension

Hypertension	Mean duration of ART	95% confidence interval
Yes	9.3825±3.14	(7.4866-11.2783)
No	9.4328±3.04	(8.4178-10.4479)

P value=0.9596

Using two sample T test with equal variances,P value of 0.9596 was computed and the mean duration of ART was found to be not statistically different in groups who developed hypertension and those who did not.

DYSLIPIDEMIA

Dyslipidemia was prevalent in 31 out of 50 patients which amounts to 62% of the total number.

All patients with dyslipidemia were above the age of 40 years.

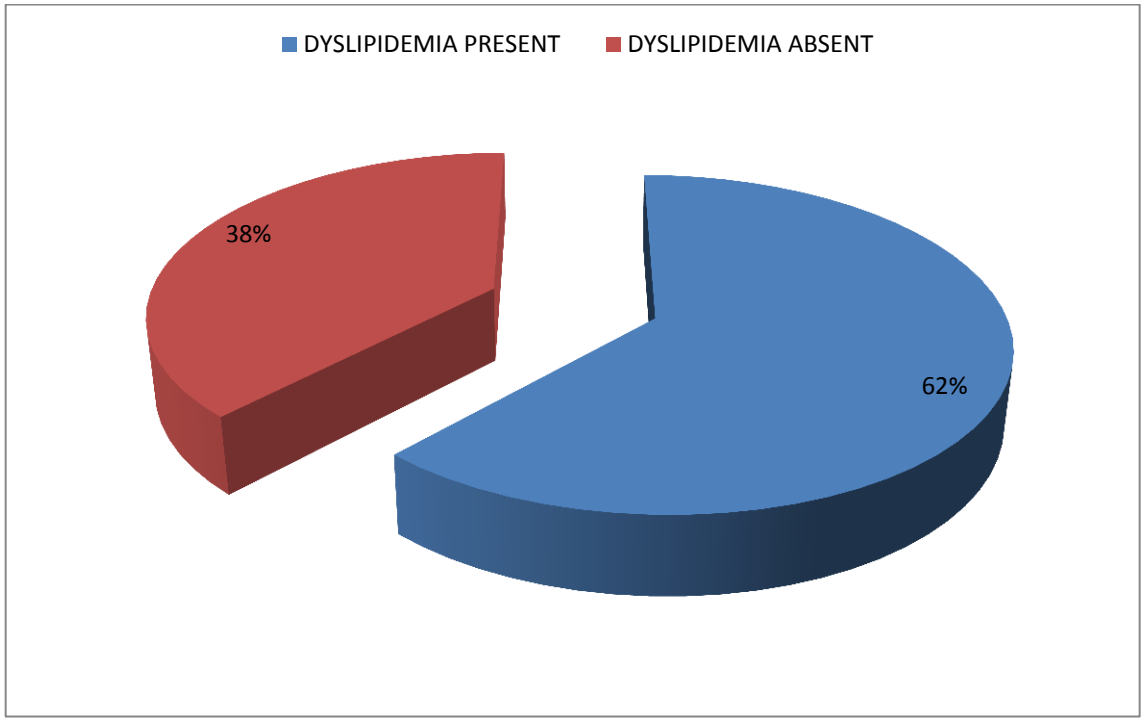


Figure 10-Distribution of dyslipidemia among study population

The comparison of ART drug group with dyslipidemia is as follows.

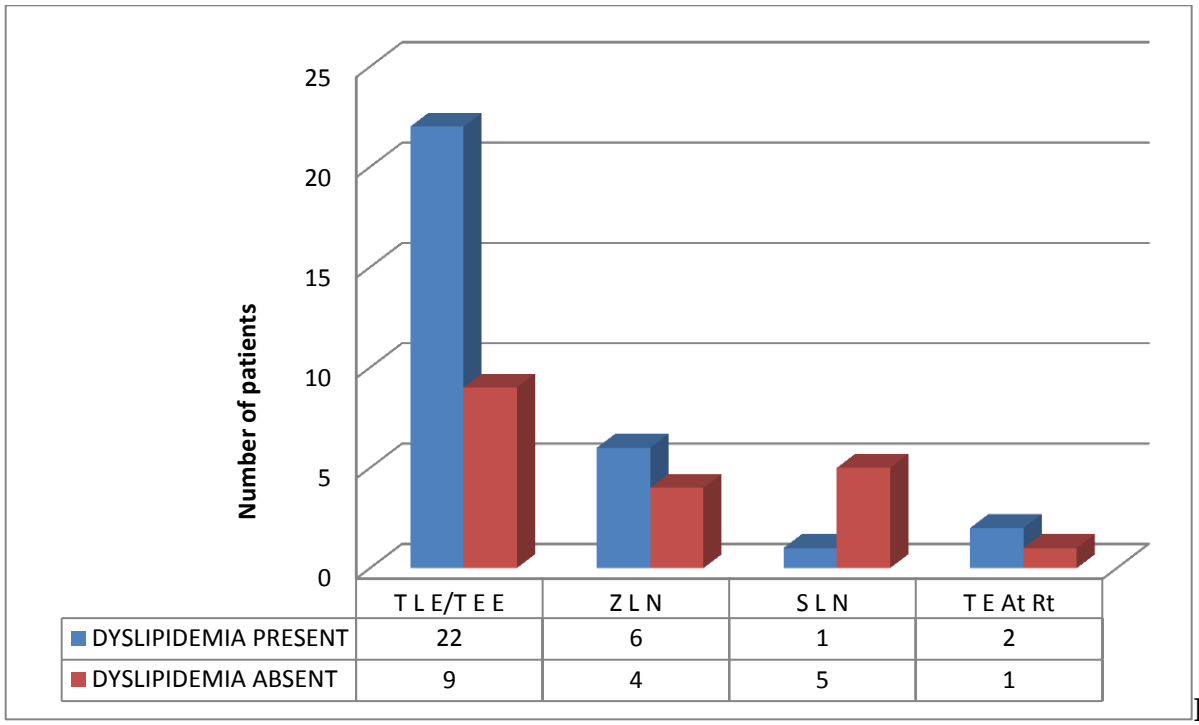


Figure 11-Comparison of ART drug group with dyslipidemia

22 patients from TEE//TLE group were found to have dyslipidemia out of the total 31 patients which constitute 70.97%.Out of the 10 patients in ZLN group,6 had dyslipidemia and 1 out of 5 patients in SLN group had dyslipidemia. 2 out of 3 (66.67%) patients in T E At Rt group also had dyslipidemia.

Table 5-Comparison of ART drug group with dyslipidemia

Dyslipidemia	TEE/TLE	ZLN/SLN	T E At Rt	Total
Yes	22(70.97%)	7(43.75%)	2(66.67%)	31
No	9(29.03)	9(56.25)	1(33.33%)	19
Total	31(100%)	16(100%)	3(100%)	50(100%)

Pearson chi2=3.3084 P value=0.069

Although there is no statistically significant association between type of drug group and dyslipidemia,the increased number of dyslipidemic patients among the recruited sample,especially in the TEE/TLE group and two thirds of patients in the T E At Rt group having dyslipidemia, is worth mentioning.

Table 6-Duration of ART versus dyslipidemia

Dyslipidemia	Mean duration of ART	95% confidence interval
Yes	9.42±3.33	(8.1987-10.6481)
No	9.41±2.55	(8.1829-10.6446)

P value=0.9915

Using two sample T test with equal variances,P value of 0.9915 was computed and the mean duration of ART was found to be not statistically different in groups who developed hypertension and those who did not.

CHRONIC KIDNEY DISEASE

Only 4 out of 50 patients were found to have chronic kidney disease.

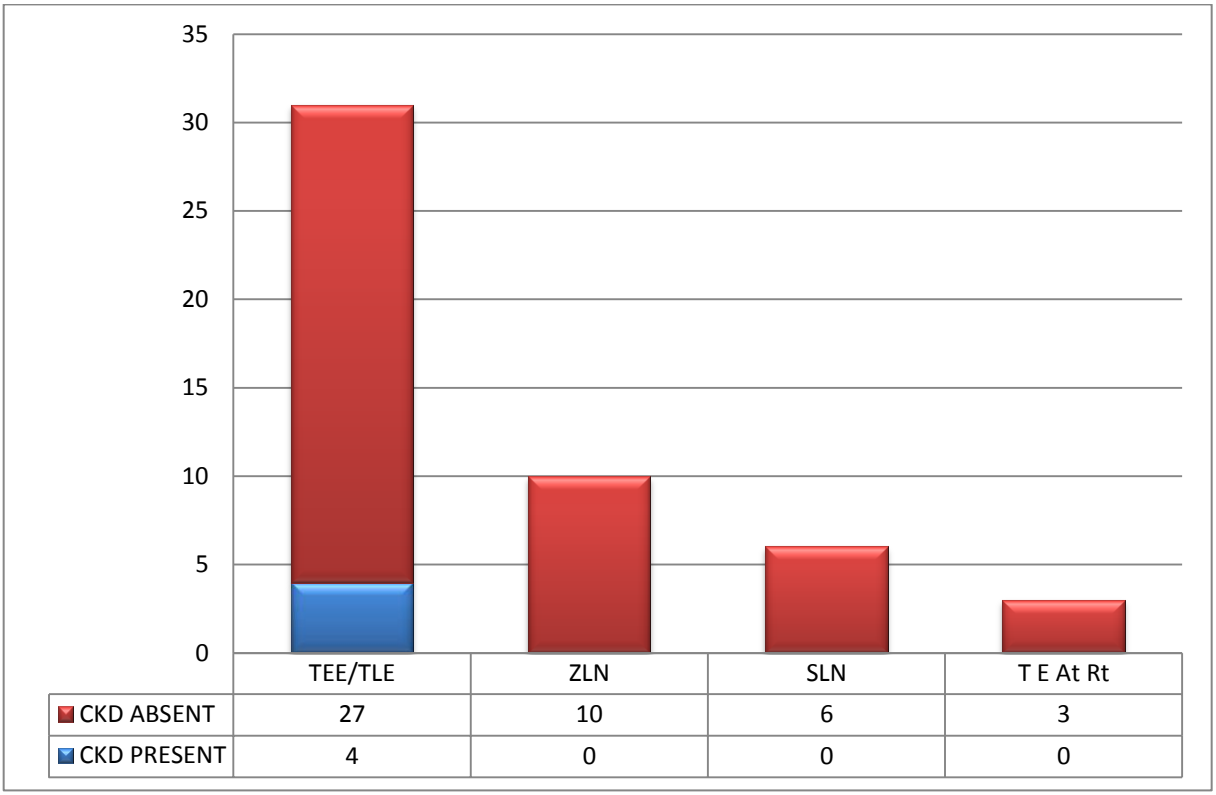


Figure 12-Comparison of ART drug group with CKD

However it is noted that all patients who had CKD belonged to the TEE/TLE group.

All four patients were above 50 years of age and all were males.

Two among the four patients had been on ART for more than 10 years,one had been on ART for 8 years and the last patient 5 years.

Table 7-Comparison of ART drug group with CKD.

CKD	TEE/TLE	ZLN/SLN	T E At Rt	Total
Yes	4(12.9%)	0(0%)	0 (0%)	4 (8%)
No	27(87.1%)	16(100%)	3 (100%)	46 (92%)
Total	31(100%)	16(100%)	3(100%)	50(100%)

Pearson chi2=2.2566 P value=0.133

There was no statistically significant association between type of ART drug and chronic kidney disease among the recruited sample of patients.

Table 8-Duration of ART versus CKD

CKD	Mean duration of ART	95% confidence interval
Yes	8.55±2.38	(4.7587-12.3332)
No	9.50±3.10	(8.5761-10.4153)

P value=0.5540

Using two sample T test with equal variances,P value of 0.5540 was computed and the mean duration of ART was found to be not statistically different in groups who developed chronic kidney disease and those who did not.

ISCHEMIC HEART DISEASE

Table 9-Characteristics of patients with IHD in the study population

AGE	ART GROUP	DURATION OF ART	OTHER COMORBID ILLNESSES	SMOKING STATUS
54	ZLN	>10 years	Dyslipidemia	Never smoker
65	TEE	5-10 years	Diabetes, Hypertension, Dyslipidemia	Former smoker
54	TLE	5-10 years	Diabetes, Hypertension, Dyslipidemia	Former smoker
53	TEE	5-10 years	Hypertension, Dyslipidemia,CKD	Former smoker
48	ZLN	>10 years	Diabetes,Hypertension,Dyslipidemia	Never smoker

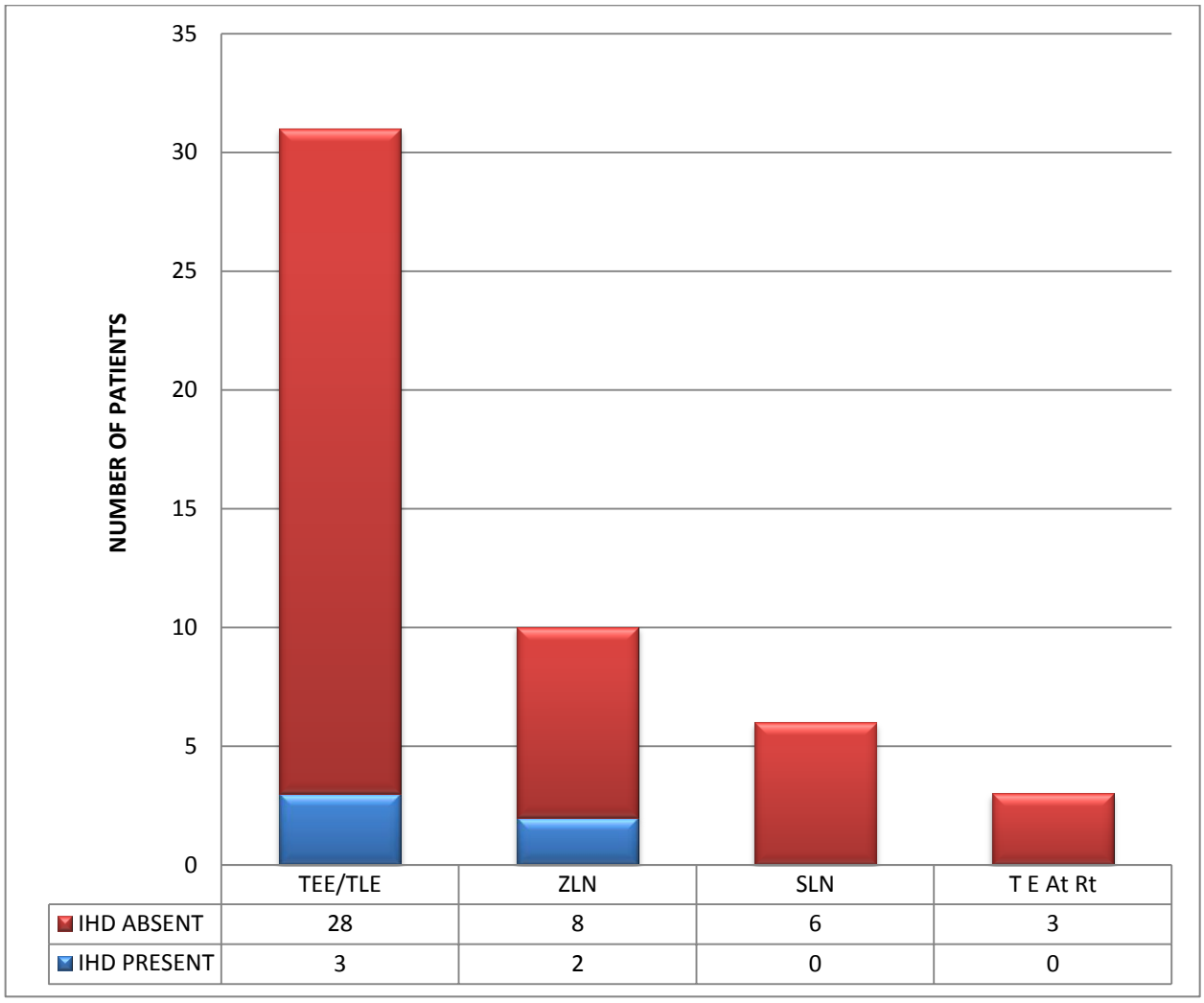


Figure 13-Comparison of ART group with IHD

5 out of the 50 patients were found to have ischemic heart disease, of which 3 were in TEE/TLE group and 2 were in the ZLN group.

Table 10- Comparison of ART group with IHD

IHD	TEE/TLE	ZLN/SLN	T E At Rt	Total
Yes	3(9.68%)	2(12.5%)	0(0%)	5 (10%)
No	28(90.32%)	14(87.5%)	3 (100%)	45 (90%)
Total	31(100%)	16(100%)	3(100%)	50(100%)

Pearson chi2=0.0884 P value= 0.766

There was no statistically significant association between type of ART drug and ischemic heart disease among the recruited sample of patients.

Table 11-Duration of ART versus IHD

IHD	Mean duration of ART	95% confidence intervals
Yes	9.09±4.55	(3.4405-14.7297)
No	9.46±2.89	(8.5874-10.3264)

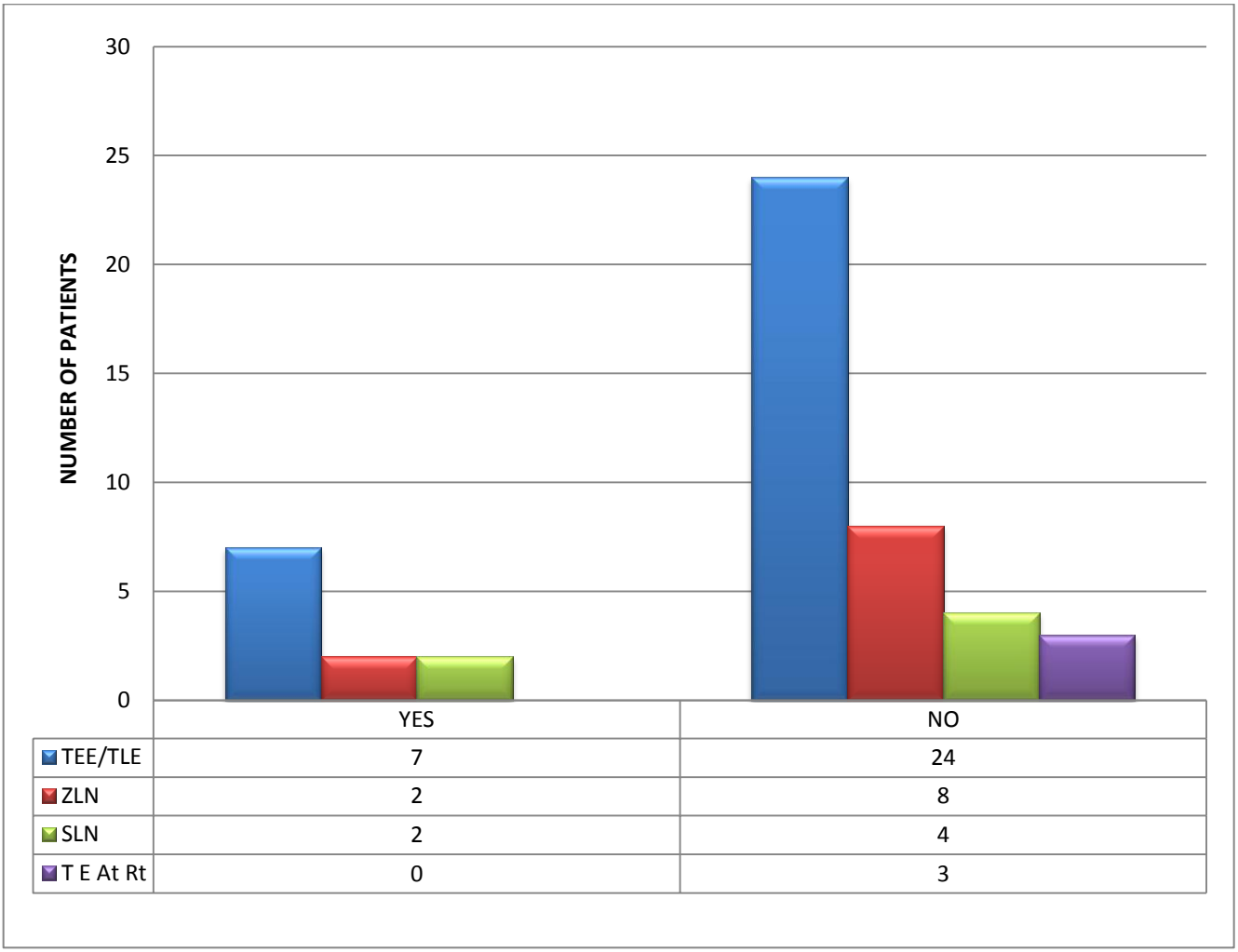
P value=0.7981

Using two sample T test with equal variances,P value of 0.7981 was computed and the mean duration of ART was found to be not statistically different in groups who developed ischemic heart disease and those who did not.

OSTEOPOROSIS

Table 12-Characteristics of patients with osteoporosis in the study population

PATIENT	AGE	GENDER	ART GROUP	DURATION OF ART
1	52	Female	SLN	>10 years
2	40	Female	TEE	>10 years
3	49	Male	ZLN	5-10 years
4	54	Male	ZLN	5-10 years
5	52	Male	TLE	>10 years
6	44	Male	TEE	>10 years
7	54	Male	TEE	>10 years
8	56	Male	TEE	>10 years
9	63	Female	TEE	5-10 years
10	39	Female	SLN	>10 years
11	62	Male	TEE	5-10 years



	YES	NO
TEE/TLE	7	24
ZLN	2	8
SLN	2	4
T E At Rt	0	3

Figure 14-Comparison of ART group with osteoporosis

11 out of the 50 patients were found to have osteoporosis,which amounts to 23.4%.

7 belonged to TEE/TLE group, 2 belonged to ZLN group and 2 belonged to SLN group. Among these 11 patients,7 were males and 4 were females.7 patients had received ART for more than 10 years while 4 had received ART for 5 to 10 years.

Table 13-Comparison of ART group with osteoporosis

Osteoporosis	TEE/TLE	ZLN/SLN	T E At Rt	Total
Yes	7(22.58%)	4(25%)	0(0%)	11(22%)
No	24_77.42%)	12(75%)	3(100%)	39(78%)
Total	31(100%)	16(100%)	3(100%)	50(100%)

Pearson chi2= 0.0345 P value=0.853

There was no statistically significant association between type of ART drug and osteoporosis among the recruited sample of patients.

Table 14-Duration of ART versus osteoporosis

Osteoporosis	Mean duration of ART	95% confidence intervals
Yes	10.82±3.23	(8.6496-12.9897)
No	9.02±2.90	(8.0844-9.9653)

P value=0.0833

Using two sample T test with equal variances, P value of 0.0833 was computed and the mean duration of ART was found to be not statistically different in groups who developed osteoporosis and those who did not.

METABOLIC SYNDROME

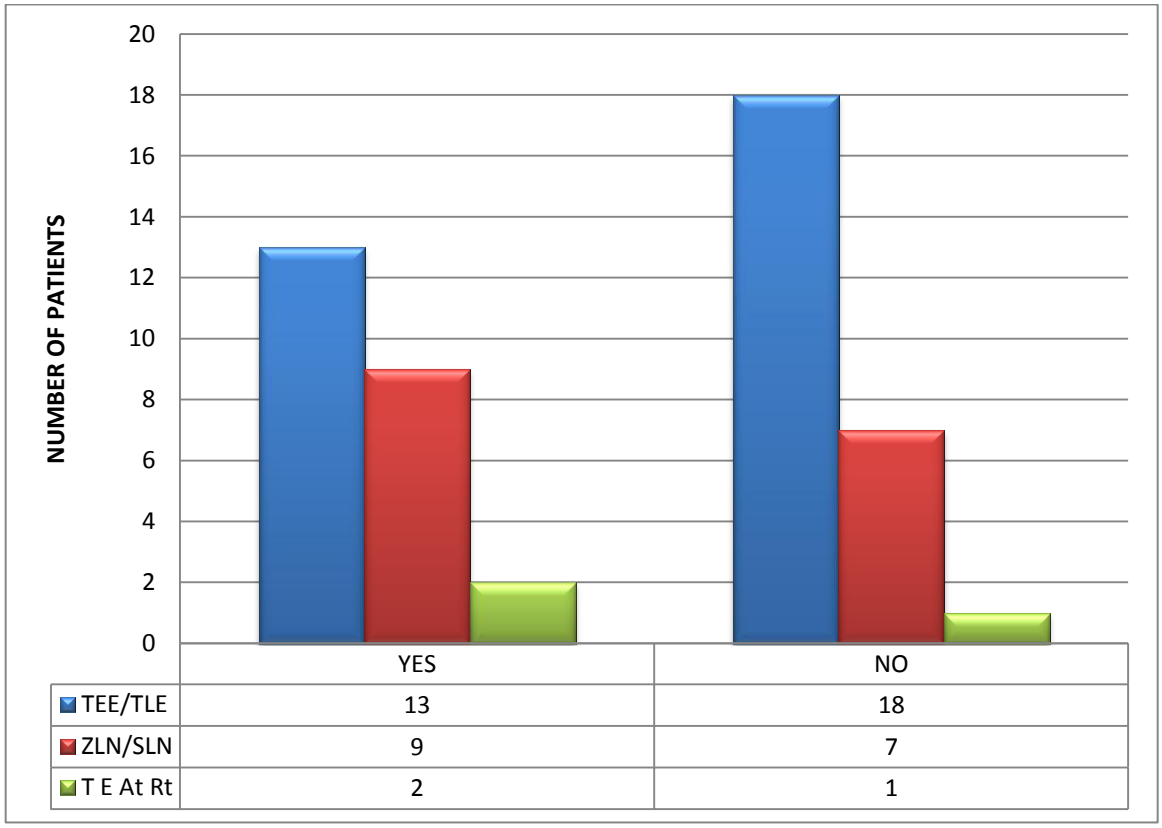


Figure 15-Comparison of ART drug group with metabolic syndrome

24 out of the 50 patients were found to satisfy the criteria for metabolic syndrome as per standard guidelines which amounts to 48% of the total patients.

Table 15- Comparison of ART drug group with metabolic syndrome

Metabolic syndrome	TEE/TLE	ZLN/SLN	T E At Rt	Total
Yes	13(41.94%)	9(56.25%)	2(66.67%)	24(48%)
No	18(58.06%)	7(43.75)	1(33.33%)	26(52%)
Total	31(100%)	16(100%)	3(100%)	50(100%)

Pearson chi2=0.8685 P value=0.351

A large proportion(48%) of the patients were found to be diagnosed with metabolic syndrome which was distributed among all the ART drug groups.

Table 16-Duration of ART versus metabolic syndrome

Metabolic syndrome	Mean duration of ART	95% confidence intervals
Yes	9.050±2.66	(7.9280-10.1724)
No	9.760±3.36	(8.4017-11.1200)

P value=0.4140

Using two sample T test with equal variances,P value of 0.4140 was computed and the mean duration of ART was found to be not statistically different in groups who developed metabolic syndrome and those who did not.

In our study it was also found that none of the patients had evidence of lipodystrophy or stroke as per the criteria used(described in annexure).

6.4 ASSESSMENT OF THE ADEQUACY OF TREATMENT

ADEQUACY OF DIABETIC CONTROL

3 different values of HbA1c were taken at different points of time and the average was calculated to assess the adequacy of treatment.If the average Hba1c was less than or equal to 7,it was considered as adequate control and if more than 7,it was considered not well controlled.

11 out of the 20 patients were found have adequate control for diabetes which constituted 55% of the diabetics in the population.

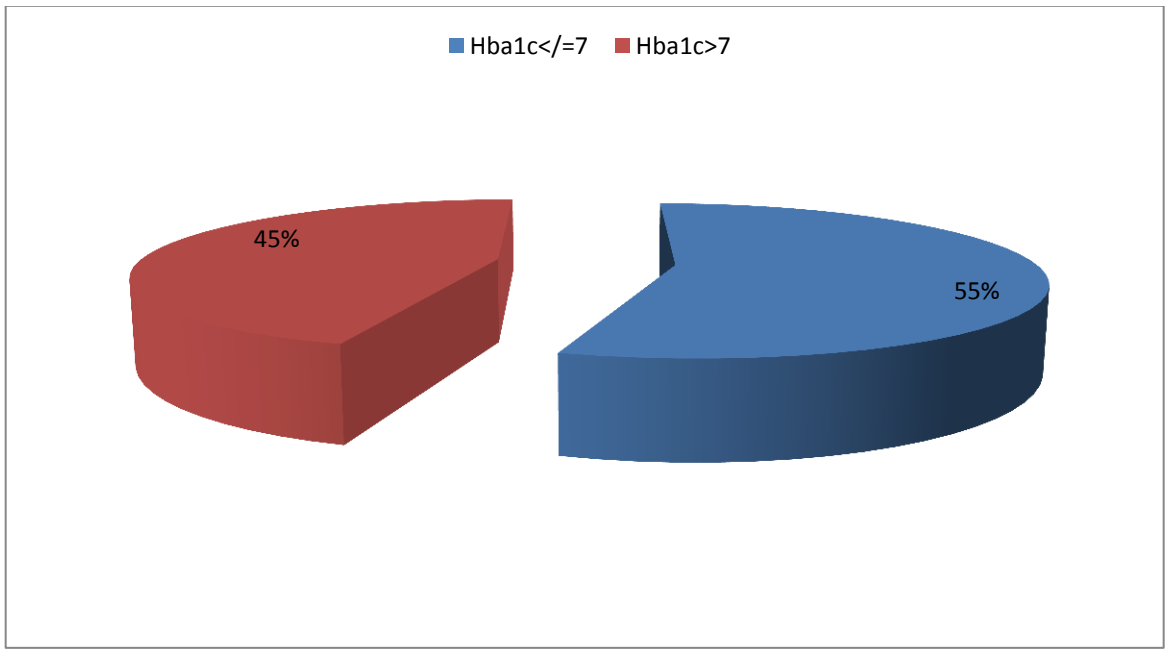


Figure 16-Adequacy of control of diabetes

ADEQUACY OF CONTROL OF HYPERTENSION

3 different blood pressure recordings at different points of time were taken and the average of the 3 values were calculated.If the average value was less than 140/90mmhg it was considered adequately controlled and if more than or equal to 140/90mmhg it was considered not well controlled.

9 out of the 13 patients who were found to have hypertension were found to be adequately controlled and 4 of them were not adequately controlled.

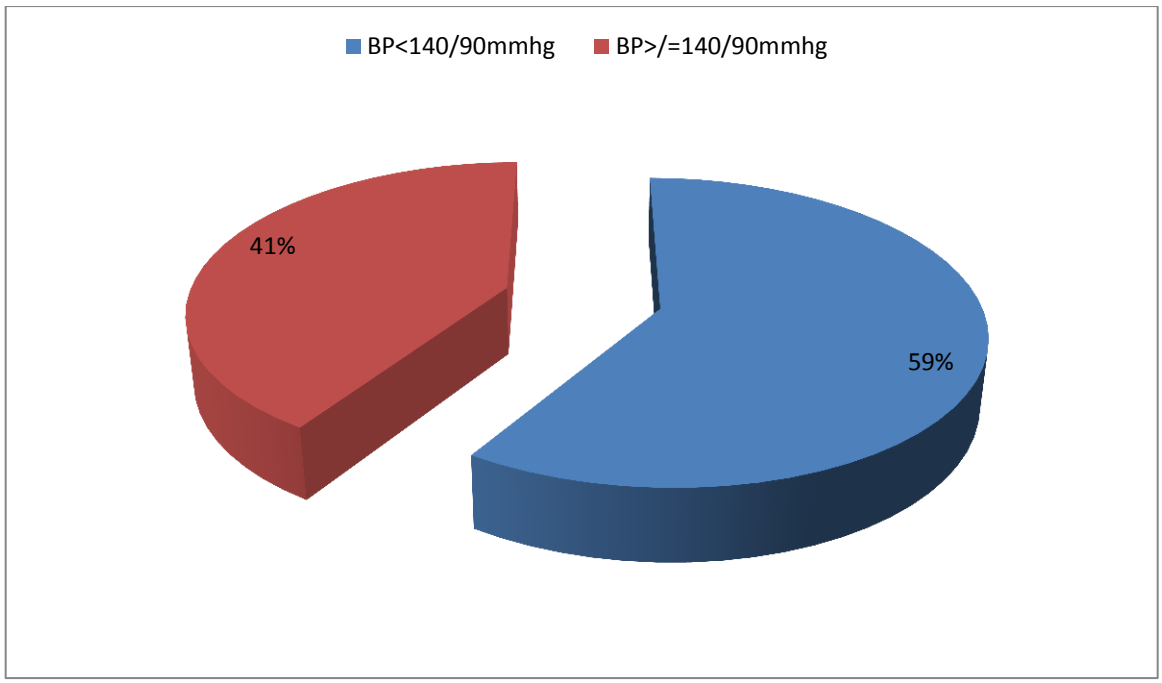


Figure 17-Adequacy of control of hypertension

ADEQUACY OF CONTROL OF DYSLIPIDEMIA

3 different LDL values at different points of time were taken and the average of the 3 values were calculated.If the average value was less than 100mg/dL it was considered adequately controlled and if more than or equal to 100mg/dL it was considered not well controlled.

Only 12 out of the 31 patients with dyslipidemia were found to have LDL<100 and hence was considered adequately controlled.19 patients had LDL levels above or equal to 100 indicating lack of adequate control.

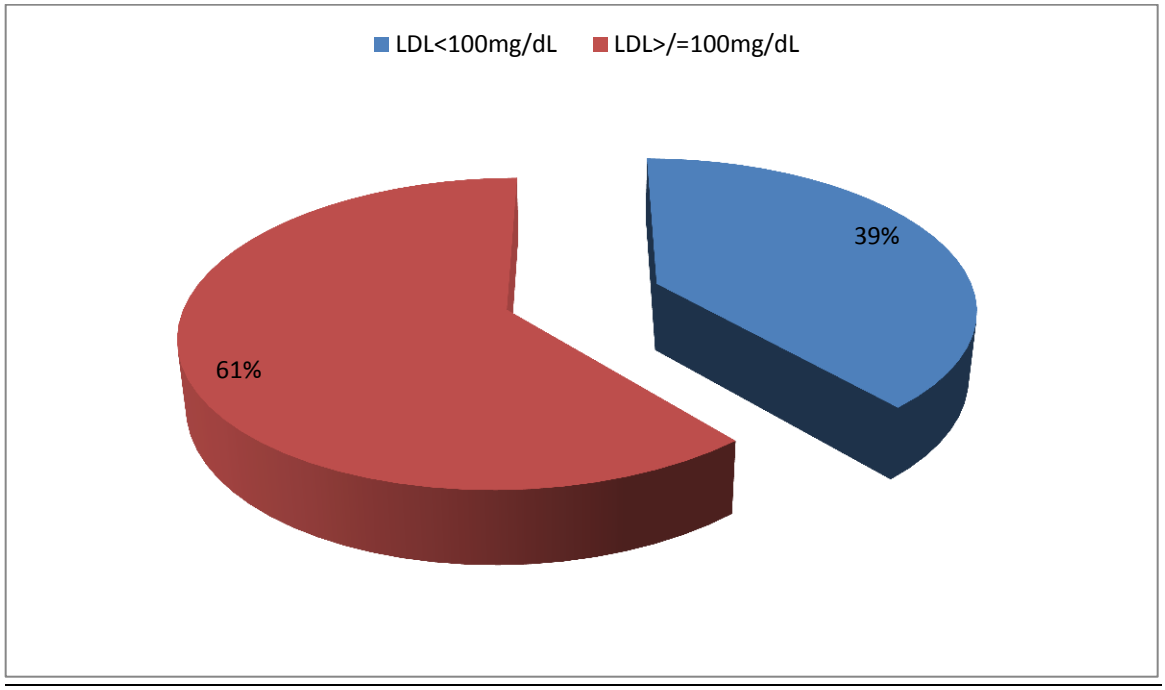


Figure 18-Adequacy of control of dyslipidemia

6.4 ASSESSMENT OF CARDIOVASCULAR RISK

Cardiovascular risk was calculated using American Heart Association Guidelines-2013 calculator.

41 patients were assessed for cardiovascular risk.The remainder 9 patients could not be included as their ages were less than 40 years and the minimum age required for using the calculator is 40 years.

The mean cardiovascular risk obtained was 10.37 ± 8.32.

When cardiovascular risk was compared with ART drug groups,the results obtained were:

ART drug group	Mean cardiovascular risk (%)	Number of patients in each drug group
TEE/TLE	12.57±9.02	26
ZLN/SLN	6.23±5.48	12
T E At Rt	7.8%±5.27	3

P value=0.03138

Patients in TEE/TLE group had an average cardiovascular risk of 12.57±9.02 % which was found to be statistically significant as well.The fact that there is statistically significant

increase of cardiovascular risk in this group and that the adequacy of control of dyslipidemia is only 39% for the overall study population is unfortunate and indicates the need of aggressive control of cardiovascular risk factors.

6.5 ASSESSMENT OF QUALITY OF LIFE INDEX

The mean total QOL was found to be 75.91± 12.3.

Individual mean domain scores were as follows.

Table 17-Individual mean domain scores of QOL

Domain	Mean score
Physical	12.36±2.76
Psychological	13.01±2.31
Level of independence	13.72±2.36
Social relationships	12.14±2.68
Environmental	12.32±2.09
Spirituality,religion,personal beliefs(SRPB)	12.36±3.12

Table 18-Comparison of ART drug group with QOL

	TEE/TLE	ZLN/SLN	T E At Rt
Total mean QOL	73.76±11.56	81.02±13.55	70.8±3.13

P value= 0.06084

There was no statistically significant association between type of ART drug and quality of life.

7. LIMITATIONS

There were a few limitations of our study which may have impacted the final result. Great care was adopted to limit the possibility of errors in this study.

1.There was no method of distinguishing between whether the direct effect of HIV and HAART led to the metabolic derangements versus the genetic and environmental factors which are already at play which could have influenced the development of the same.Our study however was not designed to account for the same.

2.The relatively small size of sample recruited could also be considered as one of the limitations.Further studies employing greater numbers are required to elicit a statistically significant association between type of ART drug as well as duration of ART with the development of the diseases of interest.

3. Since our study also included use of questionnaire, recall bias and interviewer's bias could not be avoided

8.DISCUSSION

Our study primarily aimed at assessing chronic disease profile in HIV patients on long term ART(ART more than or equal to 5 years).

20 among the 50 recruited patients were found to have diabetes based on standard guidelines,which constitute 40% of total patients which is higher than what has actually been observed in Western and Indian literature.The type of ART drug group or the duration of ART did not influence development of diabetes in our study although previous studies have shown stavudine as well as zidovudine to be associated with higher risk for development of diabetes.

Only 13 patients were found to have hypertension among the 50,which constitute 26% of total patients.The prevalence has been found to range from 7.3% to 48.2% across various studies.Here also there was no statistically significant association between type of ART drug or duration of ART in development of hypertension.

A significant proportion of patients were found to have dyslipidemia which constitute 61% of the total number . A previous study done by Carey et al from our hospital showed statistically significant increased prevalence of dyslipidemia in PLHIV on ART for more than or equal to 1 year as compared to ART naïve patients. 34% of patients on ART were found to have high LDL values as compared to 17.2% in ART naïve patients in the study.In our study which had considered a longer duration of ART(more than or equal to 5 years),the rate of dyslipidemia

was also notably higher(34% versus 61%).The mean age of patients in the study mentioned was 39.20 years while that in our study was 48.42 years.The higher age may also have influenced the rate of dyslipidemia in our study.(31)

Chronic kidney disease was found in only 4 out of 50 patients,which constitue 8% of the total patients.All four were males and all had age above 50 years.Two of them had received ART for more than 10 years.Literature shows prevalences of chronic kidney disease ranging from 7.2% to 32%. Ischemic heart disease was found in 5 out of 50 patients.All 5 patients were found to have dyslipidemia, of which 3 of them had all three risk factors:diabetes,hypertension and dyslipidemia.Two of them were non smokers and the remainder 3 were reformed smokers.

Osteoporosis was found in 11 out of 50 patients which accounts for 23.4% of the total number which was noted to be higher than values quoted in literature.63.6% patients who had osteoporosis were males.63.6% had also received a longer duration of ART(more than 10 years).

24 out of the 50 patients were found to satisfy the criteria for metabolic syndrome as per standard guidelines which amounts to 48% of the total patients. This number throws light at the fact that metabolic abnormalities are at play in patients with HIV who are on ART and adequate measures must be taken for screening,early diagnosis and treatment as well as prevention of the same in this population.

In our sample of patients we were unable to find patients who satisfied the criteria for lipodystrophy using Dual energy X ray Absorptiometry,which had a cut off of 2.28 for trunk fat by lower limb fat mass ratio.Any value more than on equal to 2.28 was considered significant,however none of the patients satisfied the criteria.

Nor were we able to find any patients with a history of or current evidence of cerebrovascular accident in our sample of patients.

With respect to secondary objectives,adequacy of treatment of diabetes,hypertension and dyslipidemia was assessed and it was found that 55% of patients with diabetes were adequately controlled .Among hypertensives,59% had adequate control .Unfortunately,although we had majority of the patients diagnosed with dyslipidemia,the control of the same among the patients was not satisfactory in terms of the fact that only 39% were having adequate control .

The assessment of cardiovascular risk in the same population showed a higher risk of 12.57±9.02% in the TEE/TLE group which was found to be statistically significant.The overall mean cardiovascular risk was 10.37±8.32. The fact that there is statistically significant increase of cardiovascular risk in this group and that the adequacy of control of dyslipidemia is only 39% for the overall study population is unfortunate and indicates the need of aggressive control of cardiovascular risk factors.

With regards to quality of life, the mean total QOL was found to be 75.91±12.3 .

The individual domain scores namely physical, psychological, level of independence, social relationships, environmental, and spirituality, religion, personal beliefs (SRPB) were uniformly found to have moderate scores.The lowest individual score was for the social relationships domain.

This is comparable with two recent studies conducted in India which was done to assess quality of life in PLHIV.(71,72)

9. CONCLUSIONS

1.Assessment of chronic disease profile in our population of PLHIV who had been on ART for more than or equal to 5 years revealed high rates of dyslipidemia(62%) followed by that of diabetes(40%).Moreover,the proportion of patients who satisfied the criteria for metabolic syndrome was also as high as 48% in the same population.

Such high rates point towards the fact that it is important to anticipate higher rates of metabolic abnormalities in this population thereby preparing ourselves for early screening and detection of the same so as to prevent complications.

Another point to note is the increased rate of osteoporosis(23.4%) in the same population which necessitates age appropriate early screening for the same so as to prevent fractures.

2. There was an increased rate of cardiovascular risk in the same population which was found to be significantly high in Tenofovir- Emtricitabine/Lamivudine-Efavirenz regimens which are unfortunately the first line agents of antiretroviral therapy used in our setting. This again calls for aggressive control of cardiovascular risk factors after early screening and detection of the same.

3. The adequacy of control of the diseases of interest as per standard guidelines ,mainly diabetes, hypertension and dyslipidemia was also not satisfactory in this population. Control of

dyslipidemia was found to be least satisfactory among the three diseases of interest. We should target at aggressive control of each of the diseases as soon as they are detected so as to mitigate cardiovascular risk.

4. The quality of life assessed in the same population showed a moderate quality of life index,the lowest individual score being that of social relationships.

10. BIBLIOGRAPHY

1. Marsden MD, Zack JA. Humanized Mouse Models for Human Immunodeficiency Virus Infection. Annu Rev Virol. 2017 Jul 26;

2. WHO | HIV/AIDS [Internet]. WHO. [cited 2017 Jul 16]. Available from: http://www.who.int/gho/hiv/en/

3. Fact sheet - Latest statistics on the status of the AIDS epidemic | UNAIDS [Internet]. [cited 2017 Jul 16]. Available from: http://www.unaids.org/en/resources/fact-sheet

4. Global HIV and AIDS statistics | AVERT [Internet]. [cited 2016 Feb 3]. Available from: http://www.avert.org/professionals/hiv-around-world/global-statistics

5. Gopal M, Bhaskaran A, Khalife WI, Barbagelata A. Heart Disease in Patients with HIV/AIDS-An Emerging Clinical Problem. Curr Cardiol Rev. 2009 May;5(2):149–54.

6. Guaraldi G, Stentarelli C, Zona S, Orlando G, Carli F, Ligabue G, et al. Lipodystrophy and anti-retroviral therapy as predictors of sub-clinical atherosclerosis in human immunodeficiency virus infected subjects. Atherosclerosis. 2010 Jan;208(1):222–7.

7. Basavaraj KH, Navya MA, Rashmi R. Quality of life in HIV/AIDS. Indian J Sex Transm Dis. 2010;31(2):75–80.

8. B. Coll, S. Parra, C. Alonso-Villaverde et al., “The role of immunity and inflammation in the progression of atheroscle- rosis in patients with HIV infection,” Stroke ,vol.38,no.9,pp. 2477–2484, 2007. -

9. Grunfeld C, Pang M, Doerrler W, Shigenaga JK, Jensen P, Feingold KR. Lipids, lipoproteins, triglyceride clearance, and cytokines in human immunodeficiency virus infection and the acquired immunodeficiency syndrome. J Clin Endocrinol Metab. 1992 May;74(5):1045–52.

10. O'Brien SJ, Moore JP. The effect of genetic variation in chemokines and their receptors on HIV transmission and progression to AIDS. Immunol Rev. 2000 Oct;177:99–111.

11. Alonso-Villaverde C, Coll B, Parra S, Montero M, Calvo N, Tous M, et al. Atherosclerosis in Patients Infected With HIV Is Influenced by a Mutant Monocyte Chemoattractant Protein-1 Allele. Circulation. 2004 Oct 12;110(15):2204–9.

12. Characterization of fractalkine (CX3CL1) and CX3CR1 in human coronary arteries with native atherosclerosis, diabetes mellitus, and transplant vascular disease | Bruce McManus - Academia.edu [Internet]. [cited 2017 Jul 28]. Available from: http://www.academia.edu/14404316/Characterization_of_fractalkine_CX3CL1_and_CX3CR1_in_human_coronary_arteries_with_native_atherosclerosis_diabetes_mellitus_and_transplant_vascular_disease

13. Kaplan RC, Kingsley LA, Gange SJ, Benning L, Jacobson LP, Lazar J, et al. Low CD4+ T cell count as a major atherosclerosis risk factor in HIV-infected women and men. AIDS Lond Engl. 2008 Aug 20;22(13):1615–24.

14. Human Immunodeficiency Virus Type 1 (HIV-1) Accessory Protein Vpr Induces Transcription of the HIV-1 and Glucocorticoid-Responsive Promoters by Binding Directly to

p300/CBP Coactivators [Internet]. [cited 2017 Jul 28]. Available from: http://jvi.asm.org/content/76/19/9724.short

15. The HIV protease inhibitor saquinavir impairs lipid metabolism and glucose transport in cultured adipocytes [Internet]. [cited 2017 Jul 28]. Available from: http://joe.endocrinology-journals.org/content/172/1/155

16. Liang J-S, Distler O, Cooper DA, Jamil H, Deckelbaum RJ, Ginsberg HN, et al. HIV protease inhibitors protect apolipoprotein B from degradation by the proteasome: A potential mechanism for protease inhibitor-induced hyperlipidemia. Nat Med. 2001 Dec;7(12):1327–31.

17. van Leth F, Phanuphak P, Ruxrungtham K, Baraldi E, Miller S, Gazzard B, et al. Comparison of first-line antiretroviral therapy with regimens including nevirapine, efavirenz, or both drugs, plus stavudine and lamivudine: a randomised open-label trial, the 2NN Study. The Lancet. 2004 Apr 17;363(9417):1253–63.

18. Murata H, Hruz PW, Mueckler M. The Mechanism of Insulin Resistance Caused by HIV Protease Inhibitor Therapy. J Biol Chem. 2000 Jul 7;275(27):20251–4.

19. Carr A, Samaras K, Chisholm DJ, Cooper DA. Pathogenesis of HIV-1-protease inhibitor-associated peripheral lipodystrophy, hyperlipidaemia, and insulin resistance. The Lancet. 1998 Jun 20;351(9119):1881–3.

20. Visceral abdominal-fat accumulation associated with use of indinavir - ScienceDirect [Internet]. [cited 2017 Jul 29]. Available from: http://www.sciencedirect.com/science/article/pii/S0140673697115185

21. The glucose fatty-acid cycle its role in insulin sensitivity and the metabolic disturbances of diabetes mellitus - ScienceDirect [Internet]. [cited 2017 Jul 29]. Available from: http://www.sciencedirect.com/science/article/pii/S0140673663915009

22. Gazzaruso C, Sacchi P, Garzaniti A, Fratino P, Bruno R, Filice G. Prevalence of Metabolic Syndrome Among HIV Patients. Diabetes Care. 2002 Jul 1;25(7):1253–4.

23. Wu P-Y, Hung C-C, Liu W-C, Hsieh C-Y, Sun H-Y, Lu C-L, et al. Metabolic syndrome among HIV-infected Taiwanese patients in the era of highly active antiretroviral therapy: prevalence and associated factors. J Antimicrob Chemother. 2012 Apr 1;67(4):1001–9.

24. Silva EFR da, Bassichetto KC, Lewi DS. Lipid profile, cardiovascular risk factors and metabolic syndrome in a group of AIDS patients. Arq Bras Cardiol. 2009 Aug;93(2):113–8.

25. APC-2016-0140-ver9-Naidu_2P 1..13 - 00010098_149254.pdf [Internet]. [cited 2017 Sep 10]. Available from: https://umexpert.um.edu.my/file/publication/00010098_149254.pdf

26. Shey_TOAIDJ - TOAIDJ-9-51.pdf [Internet]. [cited 2017 Sep 11]. Available from: https://benthamopen.com/contents/pdf/TOAIDJ/TOAIDJ-9-51.pdf

27. Idiculla J, Ravindra'n GD, D'Souza J, Singh G, Furruqh S. Diabetes mellitus, insulin resistance, and metabolic syndrome in HIV-positive patients in South India. Int J Gen Med. 2011;4:73–8.

28. Microsoft Word - 11.7Sanjeev Reddy92-100.pdf [Internet]. [cited 2017 Sep 11]. Available from: http://globalsciencepg.org/11.7%20SANJEEV%20REDDY%2092-100.pdf

29. Bajaj S, Tyagi SK, Bhargava A. Metabolic syndrome in human immunodeficiency virus positive patients. Indian J Endocrinol Metab. 2013;17(1):117–20.

30. Pujari SN, Dravid A, Naik E, Bhagat S, Tash K, Nadler JP, et al. Lipodystrophy and dyslipidemia among patients taking first-line, World Health Organization-recommended highly active antiretroviral therapy regimens in Western India. J Acquir Immune Defic Syndr 1999. 2005 Jun 1;39(2):199–202.

31. Carey R, Rupali P, Kattula D, Abraham O. Does first line antiretroviral therapy increase the prevalence of cardiovascular risk factors in Indian patients?: A cross sectional study. J Postgrad Med. 2013;59(4):258.

32. Brown TT, Cole SR, Li X, Kingsley LA, Palella FJ, Riddler SA, et al. Antiretroviral Therapy and the Prevalence and Incidence of Diabetes Mellitus in the Multicenter AIDS Cohort Study. Arch Intern Med. 2005 May 23;165(10):1179–84.

33. De Wit S, Sabin CA, Weber R, Worm SW, Reiss P, Cazanave C, et al. Incidence and Risk Factors for New-Onset Diabetes in HIV-Infected Patients. Diabetes Care. 2008 Jun;31(6):1224–9.

34. Ledergerber B, Furrer H, Rickenbach M, Lehmann R, Elzi L, Hirschel B, et al. Factors Associated with the Incidence of Type 2 Diabetes Mellitus in HIV-Infected Participants in the Swiss HIV Cohort Study. Clin Infect Dis. 2007 Jul 1;45(1):111–9.

35. Aberg JA, Gallant JE, Ghanem KG, Emmanuel P, Zingman BS, Horberg MA. Primary Care Guidelines for the Management of Persons Infected With HIV: 2013 Update by the HIV Medicine Association of the Infectious Diseases Society of America. Clin Infect Dis. 2014 Jan 1;58(1):e1–34.

36. Inaccuracy of haemoglobin A1c among HIV-infected men: effects of CD4 cell count, antiretroviral therapies and haematological parameters (PDF Download Available) [Internet]. [cited 2017 Sep 17]. Available from: https://www.researchgate.net/publication/280323170_Inaccuracy_of_haemoglobin_A1c_among_HIVinfected_men_effects_of_CD4_cell_count_antiretroviral_therapies_and_haematological_parameters

37. Dimala CA, Atashili J, Mbuagbaw JC, Wilfred A, Monekosso GL. Prevalence of Hypertension in HIV/AIDS Patients on Highly Active Antiretroviral Therapy (HAART) Compared with HAART-Naïve Patients at the Limbe Regional Hospital, Cameroon. PLOS ONE. 2016 Feb 10;11(2):e0148100.

38. Association between highly active antiretroviral therapy and hypertension in a large cohort of men followed from 1984 to 2003 Eric C. Seaberg a , Alvaro Mun˜oz a , Ming Lu a , Roger Detels b , Joseph B. Margolick c , Sharon A. Riddler d , Carolyn M. Williams e and John P. Phair f for the Multicenter AIDS Cohort Study - Google Search [Internet]. [cited 2016 Mar 18].

39. Zoest V, A R, Wit FW, Kooij KW, van der Valk M, Schouten J, et al. Higher Prevalence of Hypertension in HIV-1-Infected Patients on Combination Antiretroviral Therapy Is Associated With Changes in Body Composition and Prior Stavudine Exposure. Clin Infect Dis. 2016 Jul 15;63(2):205–13.

40. AIDS Reviews [Internet]. [cited 2017 Sep 18]. Available from: http://www.aidsreviews.com/resumen.php?id=1298&indice=2015172&u=unp

41. Rogalska-Płońska M, Rogalski P, Leszczyszyn-Pynka M, Stempkowska J, Kocbach P, Kowalczuk-Kot A, et al. Hypertension, dyslipidemia and cardiovascular risk in HIV infected adults in Poland. Kardiologia Pol Pol Heart J [Internet]. 2014 Jan 1 [cited 2017 Sep 18]; Available from: https://ojs.kardiologiapolska.pl/kp/article/view/KP.a2017.0148

42. Oh DH, Ahn JY, Kim SI, Kim MJ, Woo JH, Kim WJ, et al. Metabolic Complications among Korean Patients with HIV Infection: The Korea HIV/AIDS Cohort Study. J Korean Med Sci. 2017 Aug;32(8):1268–74.

43. Mukeba-Tshialala D, Nachega JB, Mutombo-Tshingwali M, Arendt V, Gilson G, Moutschen M. Obésité, hypertension artérielle, hypercholestérolémie et diabète non traités

chez les adultes infectés ou pas par le VIH à Mbuji-Mayi (République démocratique du Congo). Bull Société Pathol Exot. 2017 Jun 16;1–10.

44. Nsagha DS, Weledji EP, Assob NJC, Njunda LA, Tanue EA, kibu OD, et al. Highly active antiretroviral therapy and dyslipidemia in people living with HIV/AIDS in Fako Division, South West Region of Cameroon. BMC Cardiovasc Disord. 2015;15:95.

45. Nery MW, Martelli CMT, Turchi MD. Dyslipidemia in AIDS patients on highly active antiretroviral therapy. Braz J Infect Dis. 2011 Apr;15(2):151–5.

46. Currier JS, Lundgren JD, Carr A, Klein D, Sabin CA, Sax PE, et al. Epidemiological Evidence for Cardiovascular Disease in HIV-Infected Patients and Relationship to Highly Active Antiretroviral Therapy. Circulation. 2008 Jul 8;118(2):e29–35.

47. Freiberg MS, Chang C-CH, Kuller LH, Skanderson M, Lowy E, Kraemer KL, et al. HIV Infection and the Risk of Acute Myocardial Infarction. JAMA Intern Med. 2013 Apr 22;173(8):614–22.

48. Group TS for M of AT (SMART) S. CD4+ Count–Guided Interruption of Antiretroviral Treatment. N Engl J Med. 2006 Nov 30;355(22):2283–96.

49. Pasternak A, Bruin M, Bakker M, Berkhout B, M Prins J. High Current CD4+ T Cell Count Predicts Suboptimal Adherence to Antiretroviral Therapy. PloS One. 2015 Oct 15;10:e0140791.

50. Gardner LI, Holmberg SD, Williamson JM, Szczech LA, Carpenter CCJ, Rompalo AM, et al. Development of proteinuria or elevated serum creatinine and mortality in HIV-infected women. J Acquir Immune Defic Syndr 1999. 2003 Feb 1;32(2):203–9.

51. Szczech LA, Gange SJ, van der Horst C, Bartlett JA, Young M, Cohen MH, et al. Predictors of proteinuria and renal failure among women with HIV infection. Kidney Int. 2002 Jan;61(1):195–202.

52. Szczech LA, Hoover DR, Feldman JG, Cohen MH, Gange SJ, Goozé L, et al. Association between Renal Disease and Outcomes among HIV-Infected Women Receiving or Not Receiving Antiretroviral Therapy. Clin Infect Dis. 2004 Oct 15;39(8):1199–206.

53. Schwartz EJ, Szczech LA, Ross MJ, Klotman ME, Winston JA, Klotman PE. Highly Active Antiretroviral Therapy and the Epidemic of HIV+ End-Stage Renal Disease. J Am Soc Nephrol. 2005 Aug 1;16(8):2412–20.

54. Patel KK, Patel AK, Ranjan RR, Patel AR, Patel JK. Tenofovir-associated renal dysfunction in clinical practice: An observational cohort from western India. Indian J Sex Transm Dis. 2010;31(1):30–4.

55. Advanced chronic kidney disease, end-stage renal disease and renal death among HIV-positive individuals in Europe - Ryom - 2013 - HIV Medicine - Wiley Online Library [Internet]. [cited 2017 Sep 19]. Available from: http://onlinelibrary.wiley.com/doi/10.1111/hiv.12038/abstract;jsessionid=433C63069DB23B35157355A3B080B757.f04t01

56. Achhra A, Mocroft A, Ross M, Ryom L, Lucas G, Furrer H, et al. Kidney disease in antiretroviralnaïve HIV-positive adults with high CD4: prevalence and predictors of kidney disease at enrolment in the INSIGHT Strategic Timing of AntiRetroviral Treatment trial. HIV Med. 2015 Apr;16(0 1):55–63.

57. Jotwani V, Li Y, Grunfeld C, Choi AI, Shlipak MG. Risk Factors for ESRD in HIV-Infected Individuals: Traditional and HIV-Related Factors. Am J Kidney Dis. 2012 May;59(5):628–35.

58. Brown TT, McComsey GA, King MS, Qaqish RB, Bernstein BM, da Silva BA. Loss of bone mineral density after antiretroviral therapy initiation, independent of antiretroviral regimen. J Acquir Immune Defic Syndr 1999. 2009 Aug 15;51(5):554–61.

59. Duvivier C, Kolta S, Assoumou L, Ghosn J, Rozenberg S, Murphy RL, et al. Greater decrease in bone mineral density with protease inhibitor regimens compared with nonnucleoside reverse transcriptase inhibitor regimens in HIV-1 infected naive patients. AIDS Lond Engl. 2009 Apr 27;23(7):817–24.

60. Comparison of Changes in Bone Density and Turnover with Abacavir-Lamivudine versus Tenofovir-Emtricitabine in HIV-Infected Adults: 48-Week Results from the ASSERT Study [Internet]. [cited 2016 Mar 19]. Available from: http://cid.oxfordjournals.org/content/51/8/963.abstract?ijkey=3209c0c8d57feb3408053690fa79e446b8f056d1&keytype2=tf_ipsecsha

61. Gallant JE, Staszewski S, Pozniak AL, DeJesus E, Suleiman JMAH, Miller MD, et al. Efficacy and safety of tenofovir DF vs stavudine in combination therapy in antiretroviral-naive patients: a 3-year randomized trial. JAMA. 2004 Jul 14;292(2):191–201.

62. Bedimo R, Maalouf NM, Zhang S, Drechsler H, Tebas P. Osteoporotic fracture risk associated with cumulative exposure to tenofovir and other antiretroviral agents. AIDS. 2012 Apr 24;26(7):825–831.

63. Battalora L, Buchacz K, Armon C, Overton ET, Hammer J, Patel P, et al. Low bone mineral density and risk of incident fracture in HIV-infected adults. Antivir Ther. 2016;21(1):45–54.

64. Mazzotta E, Ursini T, Agostinone A, Di Nicola AD, Polilli E, Sozio F, et al. Prevalence and predictors of low bone mineral density and fragility fractures among HIV-infected patients at one Italian center after universal DXA screening: sensitivity and specificity of current guidelines on bone mineral density management. AIDS Patient Care STDs. 2015 Apr;29(4):169–80.

65. Tsai M-S, Hung C-C, Liu W-C, Chen K-L, Chen M-Y, Hsieh S-M, et al. Reduced bone mineral density among HIV-infected patients in Taiwan: prevalence and associated factors. J Microbiol Immunol Infect Wei Mian Yu Gan Ran Za Zhi. 2014 Apr;47(2):109–15.

66. Gallant JE, Staszewski S, Pozniak AL, DeJesus E, Suleiman JMAH, Miller MD, et al. Efficacy and safety of tenofovir DF vs stavudine in combination therapy in antiretroviral-naive patients: a 3-year randomized trial. JAMA. 2004 Jul 14;292(2):191–201.

67. Tungsiripat M, O'Riordan MA, Storer N, Harrill D, Ganz J, Libutti D, et al. Subjective Clinical Lipoatrophy Assessment Correlates with DEXA-measured limb fat. HIV Clin Trials. 2009;10(5):341.

68. Gallant JE, DeJesus E, Arribas JR, Pozniak AL, Gazzard B, Campo RE, et al. Tenofovir DF, emtricitabine, and efavirenz vs. zidovudine, lamivudine, and efavirenz for HIV. N Engl J Med. 2006 Jan 19;354(3):251–60.

69. Mallal SA, John M, Moore CB, James IR, McKinnon EJ. Contribution of nucleoside analogue reverse transcriptase inhibitors to subcutaneous fat wasting in patients with HIV infection. AIDS Lond Engl. 2000 Jul 7;14(10):1309–16.

70. Haubrich RH, Riddler SA, DiRienzo AG, Komarow L, Powderly WG, Klingman K, et al. Metabolic Outcomes in a Randomized Trial of Nucleoside, Nonnucleoside and Protease Inhibitor-Sparing Regimens for Initial HIV Treatment. AIDS Lond Engl. 2009 Jun 1;23(9):1109–18.

71. Anand D, Puri S, Mathew M. Assessment of Quality of Life of HIV-Positive People Receiving ART: An Indian Perspective. Indian J Community Med Off Publ Indian Assoc Prev Soc Med. 2012;37(3):165–9.

72. Ganesh Shanmugasundaram Anusuya,PM Udayashankar,Valan A S et al-International Journal of Medical and Applied sciences- original research article Quality of life of people living with hiv/aids : a cross sectional study in a community care centre in Chennai, South India .

73. Maimaiti R, Yuexin Z, Kejun P, Wubili M, Lalanne C, Duracinsky M, et al. Assessment of Health-Related Quality of Life among People Living with HIV in Xinjiang, West China. J Int Assoc Provid AIDS Care. 2017 Jan 1;2325957417729752.

74. Herrmann S, McKinnon E, Hyland NB, Lalanne C, Mallal S, Nolan D, et al. HIV-related stigma and physical symptoms have a persistent influence on health-related quality of life in Australians with HIV infection. Health Qual Life Outcomes. 2013 Apr 8;11:56.

75. Human immunodeficiency virus-associated lipodystrophy: an objective definition based on dual-energy x-ray absorptiometry-derived regional fat ratios in a South Asian population-Asha HS, Seshadri MS, Paul TV, Abraham OC, Rupali P, Thomas N-Endocrine Practice: March 2012, Vol. 18, No. 2, pp. 158-169.

11.ANNEXURES

ANNEXURE 1-CLINICAL RESEARCH FORM

SERIAL NO. ☐ CONTACT NO. ☐

SOCIO-DEMOGRAPHIC DETAILS:

NAME ☐ AGE ☐

HOSPITAL NO. ☐

Gender: 1) Male ☐ 2) Female ☐

ADDRESS:

EDUCATION : 1) Illiterate 2)Primary school 3)Middle school 4)High school 5)Intermediate or Post-high school diploma 6)Graduate or post graduate 7)Profession or honours

OCCUPATION: 1) Unemployed 2) Unskilled 3) Semiskilled 4) Skilled 5) Clerical, shop owner, farmer 6) Semi – profession 7) Profession

TREATMENT DETAILS:

Date of initiation of ART:

Details of drugs in ART:

PAST HISTORY OF OR TREATMENT FOR :

1) Diabetes	1) YES 2) NO
2) Hypertension	1) YES 2) NO
3) Dyslipidemia	1) YES 2) NO
4) Chronic kidney disease	1)YES 2)NO
5)Ischaemic heart disease	1)YES 2)NO
6)Stroke	1)YES 2)NO
7)Osteoporosis	1)YES 2)NO
8)Symptomatic carotid artery disease	1)YES 2)NO

9)Peripheral occlusive vascular disease 1)YES 2)NO

10)Abdominal aortic aneurysm 1)YES 2)NO

If yes date of diagnosis of each of the above to be mentioned.

FAMILY HISTORY OF :

Diabetes 1) YES 2)NO

Hypertension 1)YES 2)NO

Dyslipidemia 1)YES 2)NO

Ischaemic heart disease 1)YES 2)NO

Stroke 1)YES 2)NO

SMOKING:

a) What is your smoking status? 1)Never smoker 2)Past smoker 3)Current smoker

b) If 2) or 3) of a, smoking pack years? 1)< 10 2)>= 10

c) If 2) of a, number of years since quitting smoking? 1)<20 2)>= 20

ALCOHOL :

a) What is your drinking status? 1)Lifetime abstainer 2)Non-current drinker 3)Current drinker

b) For how many years have you been drinking?

c) If 2) or 3) of a, how often do you drink per week? 1) Once a week 2) 2 – 6 days a week 3)Daily

d) If 2) or 3) of a, alcohol consumed in grams per drinking day? 1) <= 30g 2)>= 30g

CLINICAL EXAMINATION:

1) Blood pressure systolic (mmHg) :
2) Blood pressure diastolic(mmHg) :

3) Waist circumference :

1) Central obesity present 2)No central obesity

1: >= 90cm(men), >=80cm (women)

2: < 90cm (men), <80cm (women)

4) Height (cm) :

5) Weight(kg):

6) Body Mass Index(kg/m2) :————

1. Underweight: BMI <18.5Kg/M²
2. Normal: BMI 18.5 to 22.9Kg/M²
3. Overweight: BMI 23 to 24.9Kg/M²
4. Obese class I: BMI 25 to 29.9Kg/M²
5. Obese class II:BMI ≥ 30Kg/M

INVESTIGATIONS

FBS

PPBS

HBA1C

FASTING LIPID PROFILE

CREATININE

UREA

ECG

DEXA SCORE 1)Osteoporosis present. 2)Osteoporosis absent

Trunk fat to lower limb fat mass ratio

1)More than or equal to 2.28-Lipodystrophy present

2) Less than 2.28-No lipodystrophy

SERIAL INVESTIGATIONS FOR ASSESSING ADEQUACY OF TREATMENT

INVESTIGATION	DATE	DATE	DATE	DATE	DATE	DATE	DATE
HBA1C							
BP RECORDING							
FASTING LDL							

ANNEXURE 2- WHO QOL HIV BREF QUESTIONNAIRE

WHOQOL-HIV BREF

MENTAL HEALTH: EVIDENCE AND RESEARCH
DEPARTMENT OF MENTAL HEALTH
AND SUBSTANCE DEPENDENCE
WORLD HEALTH ORGANIZATION
GENEVA

		Raw Score	Transformed Score	
Domain 1	(6-Q3) + (6-Q4) + Q14 + Q21 ☐ + ☐ + ☐ + ☐			
Domain 2	Q6 + Q11 + Q15 + Q24 + (6-Q31) ☐ + ☐ + ☐ + ☐ + ☐			
Domain 3	(6-Q5) + Q20 + Q22 + Q23 ☐ + ☐ + ☐ + ☐			
Domain 4	Q17 + Q25 + Q26 + Q27 ☐ + ☐ + ☐ + ☐			
Domain 5	Q12 + Q13 + Q16 + Q18 + Q19 + Q28 + Q29 + Q30 ☐ + ☐ + ☐ + ☐ + ☐ + ☐ + ☐ + ☐			
Domain 6	Q7 + (6-Q8) + (6-Q9) + (6-Q10) ☐ + ☐ + ☐ + ☐			

ABOUT YOU

Before you begin we would like to ask you to answer a few general questions about yourself: by circling the correct answer or by filling in the space provided.

What is your **gender**? Male / Female

How old are you? _____ (age in years)

What is the highest **education** you received? None at all / Primary / Secondary / Tertiary

What is your **marital status**? Single / Married/ Living as married / Separated / Divorced / Widowed

How is your **health**? Very Poor / Poor / Neither Poor nor Good / Good / Very Good

Do you consider yourself currently ill? Yes / No

If there is something wrong with you, what do you think it is? _____

Please respond to the following questions if they are applicable to you:

What is your **HIV serostatus**? Asymptomatic / Symptomatic / AIDS converted

In what year did you first test positive for HIV? _____

In what year do you think you were infected? _____

How do you believe you were **infected with HIV**? (circle one only):
Sex with a man / Sex with a woman / Injecting drugs / Blood products / Other (specify)_____

Instructions

This assessment asks how you feel about your quality of life, health, or other areas of your life. **Please answer all the questions.** If you are unsure about which response to give to a question, **please choose the one** that appears most appropriate. This can often be your first response. Please keep in mind your standards, hopes, pleasures and concerns. We ask that you think about your life **in the last two weeks**. For example, thinking about the last two weeks, a question might ask:

		Not at all	A little	A moderate amount	Very much	Extremely
11 (FS.3)	How well are you able to concentrate?	1	2	3	4	5

You should circle the number that best fits how well are you able to concentrate over the last two weeks. So you would circle the number 4 if you were able to concentrate very much. You would circle number 1 if you were not able to concentrate at all in the last two weeks.

Please read each question, assess your feelings, and circle the number on the scale for each question that gives the best answer for you.

		Very poor	Poor	Neither poor nor good	Good	Very good
1(Q1)	How would you rate your quality of life?	1	2	3	4	5

		Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
2 (Q4)	How satisfied are you with your health?	1	2	3	4	5

The following questions ask about **how much** you have experienced certain things in the last two weeks.

		Not at all	A little	A moderate amount	Very much	An extreme amount
3 (F1.4)	To what extent do you feel that physical pain prevents you from doing what you need to do?	1	2	3	4	5
4 (F50.1)	How much are you bothered by any physical problems related to your HIV infection?	1	2	3	4	5
5 (F11.3)	How much do you need any medical treatment to function in your daily life?	1	2	3	4	5
6 (F4.1)	How much do you enjoy life?	1	2	3	4	5
7 (F24.2)	To what extent do you feel your life to be meaningful?	1	2	3	4	5
8 (F52.2)	To what extent are you bothered by people blaming you for your HIV status	1	2	3	4	5
9 (F53.4)	How much do you fear the future?	1	2	3	4	5
10 (F54.1)	How much do you worry about death?	1	2	3	4	5

		Not at all	A little	A moderate amount	Very much	Extremely
11 (F5.3)	How well are you able to concentrate?	1	2	3	4	5
12 (F16.1)	How safe do you feel in your daily life?	1	2	3	4	5
13 (F22.1)	How healthy is your physical environment?	1	2	3	4	5

The following questions ask about **how completely** you experience or were able to do certain things in the last two weeks.

		Not at all	A little	Moderately	Mostly	Completely
14 (F2.1)	Do you have enough energy for everyday life?	1	2	3	4	5
15 (F7.1)	Are you able to accept your bodily appearance?	1	2	3	4	5
16 (F18.1)	Have you enough money to meet your needs?	1	2	3	4	5
17 (F51.1)	To what extent do you feel accepted by the people you know?	1	2	3	4	5
18 (F20.1)	How available to you is the information that you need in your day-to-day life?	1	2	3	4	5

19 (F21.1)	To what extent do you have the opportunity for leisure activities?	1	2	3	4	5

		Very poor	Poor	Neither poor nor good	Good	Very good
20 (F9.1)	How well are you able to get around?	1	2	3	4	5

The following questions ask you how **good or satisfied** you have felt about various aspects of your life over the last two weeks.

		Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
21 (F3.3)	How satisfied are you with your sleep?	1	2	3	4	5
22 (F10.3)	How satisfied are you with your ability to perform your daily living activities?	1	2	3	4	5
23 (F12.4)	How satisfied are you with your capacity for work?	1	2	3	4	5
24 (F6.3)	How satisfied are you with yourself?	1	2	3	4	5
25 (F13.3)	How satisfied are you with your personal relationships?	1	2	3	4	5
26 (F15.3)	How satisfied are you with your sex life?	1	2	3	4	5
27 (F14.4)	How satisfied are you with the support you get from your friends?	1	2	3	4	5
28 (F17.3)	How satisfied are you with the conditions of your living place?	1	2	3	4	5
29 (F19.3)	How satisfied are you with your access to health services?	1	2	3	4	5
30 (F23.3)	How satisfied are you with your transport?	1	2	3	4	5

The following question refers to **how often** you have felt or experienced certain things in the last two weeks.

		Never	Seldom	Quite often	Very often	Always
31 (F8.1)	How often do you have negative feelings such as blue mood, despair, anxiety, depression?	1	2	3	4	5

Did someone help you to fill out this form? _____

How long did it take to fill this form out? _____

Do you have any comments about the assessment? _____

_____

_____

_____

THANK YOU FOR YOUR HELP

ANNEXURE 3 - CONSENT FORM

Informed Consent form to participate in a research study

Study Title: Chronic disease profile of PLHIV on long term ART

Study Number: _____

Subject's Initials: _____ Subject's Name:

_____

Date of Birth / Age: _____

(Subject)

(i) I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions. [ ]

(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. [ ]

(iii) I understand that, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. [ ]

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s). [ ]

(v) I agree to take part in the above study. [ ]

Signature (or Thumb impression) of the Subject/Legally Acceptable

Date: _____/_____/_____

Signatory's Name: _____ Signature:

Or

Representative: _____

Date: _____/_____/_____

Signatory's Name: _____

Signature of the Investigator: _____

Date: _____/_____/_____

Study Investigator's Name: _____

Signature or thumb impression of the Witness: _____

Date: _____/_____/_____ Name and address of the witness _____

ANNEXURE 4- PATIENT INFORMATION SHEET

Title of research project : To study the chronic disease profile of HIV patients on long term antiretroviral therapy.

IRB protocol number:

Dr. Sumayya Abdul Kalam is conducting a study on patients presenting to Medicine 1 OPD who are on long term antiretroviral therapy(more than or equal to 5 years).We would like to invite you to be a part of this study.

This form describes what this study is about and how it will be carried out. Signing this form will mean that you have agreed to take part. Please read this form carefully and clarify any doubt that you may have regarding the study. Feel free to discuss this with your family or friends. Your participation in this study is a voluntary act and you are free to refuse participation. Your refusal to participate in this study will in no way affect your ongoing medical care and treatment in CMCH.

Purpose of this study:

This study is being carried out to study thepresence of chronic diseases like diabetes,hypertension,high blood cholesterol,chronic kidney disease,heartdisease,stroke,osteoporosis on patients who have been on long term antiretroviral therapy. By doing so, we will be able to have early detection of such diseases which will help us in early intervention,treatment and prevention of complications. We will also be measuring

the quality of life in the same population which will enable us to improve our standards of care.

By agreeing to take part, what will you have to do?

On agreeing to participate, you will be asked a few questions regarding your ART treatment, habits, and comorbidities.You will undergo a physical examination including blood pressure, height, weight, waist circumference. Relevant blood investigations will be sent. ECG will be done for all patients.Bone mineral density scan will be done for all patients.You will have to fill a questionnaire which will help in measuring your quality of life.

Potential risks and discomforts:

This study does not involve any new drug or treatment.

There are no other potential discomforts from this study.

Potential benefits:

By participating in this study you will help us tohave early detection of such diseases which will help us in early intervention,treatment and prevention of complications. We will also be measuring the quality of life in the same population which will enable us to improve our standards of care.

Voluntary participation and withdrawal:

Participation in this study is entirely voluntary and you may choose not to participate. Doing so will not affect your medical care in CMCH in any way.

Study related injury

We do not expect any injury to happen to you while participating in this study.

Payment for the study

All your investigations will be done at the standard costs prevailing in our institution at the time of conducting the study.

Confidentiality

The results of this study will be published in a medical journal but you will not be identified by name in any publication or presentation of results. However, your medical notes will be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

Legal rights

You are not waiving any of your legal rights by participating in this study or by signing this consent form, for example, the right to seek damages under law for any research related injury.

If you have further queries, kindly feel free to contact Dr. Sumayya Abdul Kalam

(Phone no 9003805715)-Medicine 1 department.

ANNEXURE 5- INSTITUTIONAL REVIEW BOARD APPROVAL

OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Alfred Job Daniel, D Ortho MS Ortho DNB Ortho.
Chairperson, Research Committee & Principal

Dr. Biju George, MBBS., MD., DM
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

May 24, 2016

Dr. Sumayya Abdul Kalam,
PG Registrar
Department of Medicine-1
Christian Medical College,
Vellore 632 004.

Sub: **Fluid Research Grant NEW PROPOSAL:**
Chronic disease profile of HIV positive patients on long term anti-retroviral therapy Dr. Sumayya Abdul Kalam, PG Registrar, Employment Number:21195, Medicine, Dr Alice Joan Mathuram, Associate Professor, Employment Number: 28529, Dr. Anand Zachariah, Professor And Head, Dr. J V Punitha, Assistant Professor, Department of General Medicine, Ms. Mahasampath Gowri S, Sr. Demonstrator Gr, Department of Biostatistics.

Ref: IRB Min No: 10024 [OBSERV] dated 04.04.2016,

Dear Dr. Sumayya Abdul Kalam,

I enclose the following documents:-

1. Institutional Review Board approval 2. Agreement

Could you please sign the agreement and send it to Dr. Biju George, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes,

Dr. Biju George
Secretary (Ethics Committee)
Institutional Review Board

Dr. BIJU GEORGE
MBBS., MD., DM.
SECRETARY - (ETHICS COMMITTEE)
Institutional Review Board,
Christian Medical College, Vellore - 632 002.

OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Alfred Job Daniel, D Ortho MS Ortho DNB Ortho.
Chairperson, Research Committee & Principal

Dr. Biju George, MBBS., MD., DM
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May 24, 2016

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Sub: **Fluid Research Grant NEW PROPOSAL:**
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Ref: IRB Min No: 10024 [OBSERV] dated 04.04.2016

Dear Dr. Sumayya Abdul Kalam,

The Institutional Review Board (Blue, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project titled "Chronic disease profile of HIV positive patients on long term anti-retroviral therapy" on April 04 2016.

The Committee reviewed the following documents:

1. IRB Application format
2. Patient Information Sheet (English, Tamil, Telugu)
3. Consent Form (English, Tamil, Telugu)
4. Curriculum Vitae of Drs. Alice, Anand zachariah, Pnitha, Mahasampath Gowri, Sowmya.
5. Proforma
6. No. of documents 1 - 5.

The following Institutional Review Board (Blue, Research & Ethics Committee) members were present at the meeting held on April 04th 2016 in the CREST/SACN Conference Room, Christian Medical College, Bagayam, Vellore 632002.

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Alfred Job Daniel, D Ortho MS Ortho DNB Ortho.
Chairperson, Research Committee & Principal

Dr. Biju George, MBBS., MD., DM
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

Name	Qualification	Designation	Affiliation
Dr. Biju George	MBBS, MD, DM	Professor, Haematology, Research), Additional Vice Principal , Deputy Chairperson (Research Committee), Member Secretary (Ethics Committee), IRB, CMC, Vellore	Internal, Clinician
Dr. Anuradha Rose	MBBS, MD, MHSC (Bioethics)	Associate Professor, Community Health, CMC, Vellore	Internal, Clinician
Dr. Jayaprakash Muliyil	BSc, MBBS, MD, MPH, Dr PH (Epid), DMHC	Retired Professor, Vellore	External, Scientist &Epidemiologist
Rev. Joseph Devaraj	BSc, BD	Chaplaincy Department, CMC, Vellore	Internal, Social Scientist
Ms. Grace Rebekha	M.Sc., (Biostatistics)	Lecturer, Biostatistics, CMC, Vellore	Internal, Statistician
Dr. Visalakshi. J	MPH, PhD	Lecturer, Biostatistics, CMC, Vellore	Internal, Statistician
Dr. Mathew Joseph	MBBS, MCH	Professor, Neurosurgery, CMC, Vellore	Internal, Clinician
Mr. Samuel Abraham	MA, PGDBA, PGDPM, M. Phil, BL.	Sr. Legal Officer, CMC, Vellore	Internal, Legal Expert
Mrs. Pattabiraman	BSc, DSSA	Social Worker, Vellore	External, Lay Person
Dr. B. J. Prashantham	MA(Counseling Psycho MA(Theology), Dr. Min(Clinical Counselling)	Chairperson, Ethics Committee, IRB. Director Christian Counseling Cen Vellore	External, Social Scientist
Dr. Rajesh Kannangai	MD, PhD.	Professor, Clinical Virology, CMC, Vellore	Internal, Clinician
Dr. Thomas V Paul	MD, DNB(Endo), Phd(Endo)	Professor, Endocrinology, CMC, Vellore	Internal, Clinician

IRB Min No: 10024 [OBSERV] dated 04.04.2016

ANNEXURE 6 - STROBE CHECKLIST

Table. **The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: Checklist of Items That Should Be Addressed in Reports of Observational Studies**

Item	Item Number	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract. (b) Provide in the abstract an informative and balanced summary of what was done and what was found.
Introduction		
Background/ rationale	2	Explain the scientific background and rationale for the investigation being reported.
Objectives	3	State specific objectives, including any prespecified hypotheses.
Methods		
Study design	4	Present key elements of study design early in the paper.
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection.
Participants	6	(a) Cohort study: Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up. Case–control study: Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls. Cross-sectional study: Give the eligibility criteria, and the sources and methods of selection of participants. (b) Cohort study: For matched studies, give matching criteria and number of exposed and unexposed. Case–control study: For matched studies, give matching criteria and the number of controls per case.
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group.
Bias	9	Describe any efforts to address potential sources of bias.
Study size	10	Explain how the study size was arrived at.
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why.
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding. (b) Describe any methods used to examine subgroups and interactions. (c) Explain how missing data were addressed. (d) Cohort study: If applicable, explain how loss to follow-up was addressed. Case–control study: If applicable, explain how matching of cases and controls was addressed. Cross-sectional study: If applicable, describe analytical methods taking account of sampling strategy. (e) Describe any sensitivity analyses.
Results		
Participants	13*	(a) Report the numbers of individuals at each stage of the study—e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed. (b) Give reasons for nonparticipation at each stage. (c) Consider use of a flow diagram.
Descriptive data	14*	(a) Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders. (b) Indicate the number of participants with missing data for each variable of interest. (c) Cohort study: Summarize follow-up time—e.g., average and total amount.
Outcome data	15*	Cohort study: Report numbers of outcome events or summary measures over time. Case–control study: Report numbers in each exposure category or summary measures of exposure. Cross-sectional study: Report numbers of outcome events or summary measures.
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence intervals). Make clear which confounders were adjusted for and why they were included. (b) Report category boundaries when continuous variables were categorized. (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period.
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions and sensitivity analyses.
Discussion		
Key results	18	Summarize key results with reference to study objectives.
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.
Generalizability	21	Discuss the generalizability (external validity) of the study results.
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based.

*Give such information separately for cases and controls in case–control studies, and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

An Explanation and Elaboration article (18–20) discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available at www.annals.org and on the Web sites of *PLoS Medicine* [www.plosmedicine.org] and *Epidemiology* [www.epidem.com]). Separate versions of the checklist for cohort, case–control, and cross-sectional studies are available on the STROBE Web site (www.strobe-statement.org).

ANNEXURE 7- DATA SET

slno	age	gender	address	education	occup	artdate	artdrugs	dm	htn	dyslip	ckd	ihd	stroke	scad	povd	aaa	famdm	famhtn	famdyslip	famihd	famstroke	smoking	smokepack
1	44	1	Varanthapuram,Vel	4	3	18/01/2011	2	2	2	1	2	2	2	2	2	2	1	2	2	2	2	2	2
2	51	1	Nellaya House,Otta	4	3	20/05/2006	5	1	2	1	2	2	2	2	2	2	1	1	2	2	2	1	
3	38	1	Rafiganj,Aurangaba	5	5	09/06/2006	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1
4	46	2	No 13,Veerapancha	3	1	03/03/2009	2	2	2	1	2	2	2	2	2	2	1	2	2	2	2	1	
5	46	1	G4,Sunny Side Hom	6	6	02/06/2010	4	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1
6	44	1	Perunthurai,Erode,	5	5	20/09/2012	7	1	2	1	2	2	2	2	2	2	1	2	2	2	2	3	2
7	56	1	Vapanapalli,Kirishna	3	4	09/10/2007	2	2	2	1	2	2	2	2	2	2	1	1	2	2	2	3	2
8	43	1	Inikonda Mandalam	4	4	05/10/2005	2	2	2	1	2	2	2	2	2	2	1	2	2	1	2	2	2
9	20	1	Ambhati Street,Vizi	5	6	02/07/2009	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	
10	52	2	Vivek gardens,Krish	2	1	03/08/2003	5	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	
11	36	2	Pavani Homes,Nellc	5	6	09/11/2007	2	2	2	2	2	2	2	2	2	2	2	2	1	2	1	1	
12	39	2	Bhyragapatted Stre	4	4	13/04/2004	5	2	2	2	2	2	2	2	2	2	2	1	2	2	2	1	
13	54	1	84 Giruba nagar,Ve	6	6	01/05/2001	4	2	2	1	2	1	2	2	2	2	1	1	1	2	2	1	
14	44	1	Orhanpur,Nawada,I	5	4	13/09/2007	5	2	2	2	2	2	2	2	2	2	1	2	2	2	2	2	1
15	51	1	Thalatheru,Karaikal	5	5	06/07/2012	7	1	2	1	2	2	2	2	2	2	2	2	2	1	2	2	2
16	45	1	Nagari,Chittoor,And	3	3	02/04/2000	4	1	1	1	2	2	2	2	2	2	1	2	2	2	2	1	
17	49	1	Solishwaran Koil Str	4	3	02/07/2011	2	1	2	1	2	2	2	2	2	2	1	1	2	2	2	2	1
18	62	1	No 37,Engineers' Co	7	7	27/07/2009	2	1	1	1	2	2	2	2	2	2	2	2	2	2	2	2	1
19	46	1	Agarala Village,Chit	3	2	05/09/2011	4	2	2	1	2	2	2	2	2	2	2	1	1	1	2	2	2
20	44	2	Vivekananda Street	4	1	06/05/2011	2	2	2	1	2	2	2	2	2	2	1	1	2	2	2	1	
21	60	2	TNHB Colony,Krishn	3	1	09/09/2010	7	1	2	2	2	2	2	2	2	2	1	1	1	2	2	1	
22	63	1	Housing Board,Krish	3	2	07/06/2009	2	1	2	1	1	2	2	2	2	2	2	2	2	2	2	2	2
23	34	2	Sennimalaipalayam	6	6	04/10/2008	4	2	2	2	2	2	2	2	2	2	1	2	2	2	1	1	
24	65	1	Madavalam,Vellore	2	2	05/01/2012	2	1	1	1	2	1	2	2	2	2	1	2	2	2	2	2	2
25	40	2	Kaveripattnam,Dha	3	1	18/04/2005	2	2	2	2	2	2	2	2	2	2	2	2	2	1	2	2	1
26	50	1	Kaveripattnam,Dha	5	4	13/07/2010	5	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1
27	46	1	Vaniyambadi,Vellor	5	3	02/01/2011	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	2	3	2
28	58	1	Sheshepiran Street,	4	3	20/10/2005	4	1	1	1	2	2	2	2	2	2	1	2	2	2	2	2	2
29	44	1	Kovur,Nellore,Andh	4	4	12/08/2003	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2
30	49	1	Aathamakur,Nellore	5	4	06/08/2010	4	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	
31	45	2	Aathamakur,Nelloe	3	1	09/07/2006	4	2	2	1	2	2	2	2	2	2	1	2	2	2	2	1	
32	55	1	Chengalapuram,Sel	5	5	04/03/2007	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	1
33	54	1	Jagsawali,Jamshedp	5	6	05/12/2009	2	1	1	1	2	1	2	2	2	2	1	2	2	2	2	2	2
34	44	1	Thuthoor,Kanyakun	7	7	25/01/2007	2	1	1	1	2	2	2	2	2	2	1	1	2	2	2	2	1
35	48	1	R R V Puram,Vizaga	6	6	02/07/2009	4	2	2	2	2	2	2	2	2	2	1	2	2	1	2	1	
36	52	1	Ganapathi Palayam	4	4	09/06/2003	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
37	57	1	Pruddatur,Kadappa	2	2	15/07/2003	2	1	2	1	2	2	2	2	2	2	2	2	2	2	2	1	
38	54	1	F/F6,Police Line,Vel	6	7	07/05/2003	2	1	2	1	2	2	2	2	2	2	1	1	2	2	2	3	2
39	53	1	Aravinda Nagar,Kak	5	5	12/01/2012	2	2	1	1	1	1	2	2	2	2	2	2	2	2	2	2	1
40	35	2	Bairagipattidi,Tirupa	6	6	15/06/2007	5	2	2	2	2	2	2	2	2	2	1	2	2	2	2	1	
41	46	1	Kabalar malai,Nama	5	5	26/12/2010	2	2	1	2	2	2	2	2	2	2	1	2	2	2	2	1	
42	52	1	A K Nagar,Nellore,A	5	6	06/05/2008	2	2	1	2	2	2	2	2	2	2	1	2	2	2	2	2	1
43	47	1	Pillaiyar Koil Street,	4	3	23/03/2011	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2
44	36	2	Ramalingapuram,N	5	5	12/04/2006	1	2	2	2	2	2	2	2	2	2	1	1	2	2	2	1	
45	41	1	Naidupet,Nellore,A	5	5	02/02/2007	1	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	1
46	60	1	Chanam Lekai,Imph	6	6	05/04/2007	2	1	1	1	1	2	2	2	2	2	2	1	2	2	2	1	
47	63	2	Chanam Leikai,Impl	5	4	07/02/2010	2	1	2	1	2	2	2	2	2	2	2	2	2	2	2	1	
48	48	1	Veerapandi P.O,Tiru	6	6	05/07/2006	4	1	1	1	2	1	2	2	2	2	1	2	2	2	2	1	
49	58	1	Nehru Nagar,Chitto	2	2	16/11/2006	2	1	1	1	1	2	2	2	2	2	2	1	2	2	2	1	
50	56	1	Chagallu,West God	5	5	21/03/2008	2	1	1	1	2	2	2	2	2	2	1	2	2	2	2	2	2

quitsmoke	alcohol	drinkyears	drinkweek	drinkday	sysbp	diasbp	waist	ht	wt	bmi	fbs	ppbs	hba1c	tc	triy	hdl	ldl	creat	urea	ecg	dexa	fatmass	hba1cd1	hba1cd2	hba1cd3
1	2	20	1	1	110	70	85	158	58	23.23	95	73	4.9	189	201	44	118	0.85	26	1	2	2			
	1				130	80	87	162	70	26.67	138	181	8	174	215	31	105	0.98	20	1	2	2	7.9	8	8
1	2	17	1	1	110	70	86	164	55	20.45	92	130	5.7	165	136	46	101	0.75	26	1	2	2	5.2	5.7	
	1				130	84	93	145	62	29.49	105	104	5.8	192	102	42	143	0.62	24	1	2	2			
1	2	15	1	1	120	70	83	174	76	25.1	119	98	7	174	268	45	108	1.36	22	1	2	2	7		
	3	20	1	1	130	80	89	170	74	25.61	181	299	8	135	56	56	78	0.79	20	1	2	2	7.7	9.9	8
	3		1	1	140	80	92	159	67	26.5	117	156	5.8	193	118	47	138	0.93	25	1	1	2	6.8	6	5.8
1	2	20	1	1	120	70	85	178	80	25.25	95	132	5.9	199	121	37	130	0.85	23	1	2	2	5.8	5.9	
	1				110	70	82	158	60	24.03	92	84	5.2	116	70	26	88	0.88	30	1	2	2			
	1				90	60	65	148	42	19.17	84	120	5.1	111	210	23	60	0.28	30	1	1	2			
	1				110	70	70	148	45	20.54	96	106	5	195	203	38	143	0.51	15	1	2	2			
	1				100	70	85	150	63	28	91	130	5.7	160	217	46	98	0.7	29	1	1	2			
	1				138	84	86	165	64	23.51	81	120	6	224	420	30	148	0.85	26	1	1	2			
1	2	5	1	1	140	70	88	163	62	23.34	88	103	5	165	165	32	108	0.71	20	1	2	2			
1	3	20	2	2	130	70	84	178	75	23.67	104	132	6.7	125	120	31	98	0.79	14	1	2	2	7.1	6.8	6.7
	1				140	90	88	178	75	23.67	141	220	6.9	178	210	36	120	0.73	20	1	2	2	6.6	7.5	6.9
2	1				128	86	92	165	61	22.41	212	299	6.4	180	297	40	68	0.71	25	1	2	2	6	7	6.4
1	1				150	90	95	160	83	32.42	128	142	6.7	185	122	43	131	0.85	24	1	1	2	8.6	7	6.7
1	2	10	1	1	140	86	94	170	87	30.1	84	140	5.5	228	126	63	139	0.86	20	1	2	2			
	1				120	80	82	150	63	28	102	144	5.1	182	128	62	115	0.5	21	1	2	2			
	1				130	70	86	158	65	26.04	139	162	6.6	178	119	45	103	0.76	27	1	2	2	7	7.2	7
2	2	30	1	1	130	80	82	165	60	22.04	397	607	9.8	163	134	46	89	1.53	34	1	2	2	7.4	8.9	9.8
	1				120	80	95	165	74	27.18	89	107	4.5	177	95	41	112	0.5	20	1	2	2			
1	2	30	1	1	110	70	86	161	60	23.15	118	133	6.2	149	240	38	77	1.07	26	2	2	2	6.8	6.7	6.2
	1				120	70	89	150	60	26.67	96	134	5.6	195	80	55	111	0.56	18	1	1	2			
	2	15	1	1	130	90	87	165	67	24.61	100	128	5.5	156	129	48	98	0.71	20	1	2	2			
1	2	20	1	1	130	70	92	165	85	31.22	93	98	5.1	135	97	34	83	0.7	20	1	2	2			
1	1				120	76	85	163	62	23.34	152	238	7	186	79	50	121	0.73	20	1	2	2	8	7.2	7
1	1				130	80	92	169	81	28.36	120	130	5.3	144	224	31	89	0.75	22	1	2	2			
	1				120	70	83	157	57	23.12	100	121	5	112	126	37	74	0.86	21	1	1	2			
	1				110	80	93	150	65	28.89	92	100	5.5	184	131	45	107	0.9	16	1	2	2			
1	2	15	1	1	130	70	86	175	75	24.49	112	134	5.4	198	341	30	121	0.88	24	1	2	2			
1	1				120	70	96	155	77	32.05	123	148	5.9	122	117	26	85	0.78	22	2	1	2	6.7	5.6	5.9
1	2	25	1	1	130	84	92	157	62	25.15	110	140	6.2	163	103	56	101	0.51	20	1	1	2	7.3	6.5	6.2
	1				120	70	85	170	66	22.84	95	142	6.2	126	91	23	77	0.77	18	1	2	2			
1	1				140	80	90	160	68	26.56	97	140	5.8	158	170	38	100	0.58	20	1	1	2			
	1				130	90	83	160	54	21.09	163	228	6.6	176	136	52	118	0.85	24	1	2	2	7.4	6.9	6.6
	3	20	1	1	130	84	88	175	64	20.9	98	263	7.7	150	244	37	91	0.92	26	1	2	2	7.5	7.3	7.7
1	1				140	90	91	169	71	24.86	100	106	5.4	201	225	41	131	1.37	20	1	2	2			
	1				120	70	79	151	55	24.12	103	118	5	177	57	49	117	0.53	20	1	2	2			
	1				160	90	93	165	83	30.49	100	126	6	136	89	32	91	5.39	40	1	2	2			
1	1				130	90	87	168	64	22.68	96	107	5.2	138	139	40	90	1.05	15	1	2	2			
1	1	25	1	1	110	70	84	173	83	27.73	94	160	6	279	138	37	217	0.83	23	1	2	2			
	1				120	80	94	157	57	23.12	90	132	5.8	150	130	44	90	0.62	20	1	2	2			
1	1				110	80	92	180	90	27.78	106	124	5.3	143	557	24	57	0.81	25	1	2	2			
	1				140	80	91	165	68	24.98	204	222	6.8	146	172	48	77	1.39	26	1	2	2	9.4	8	6.8
	1				120	90	88	154	59	24.88	105	156	6	182	105	63	111	0.76	24	1	1	2	7	6.2	6
	1				130	90	95	170	90	31.14	205	323	8.5	241	305	41	152	0.71	14	2	2	2	7	8	8.5
	1				140	80	94	164	88	32.72	110	180	8	175	75	56	99	1.35	26	1	2	2	6.2	6	8
1	2	30	1	1	130	84	95	169	87	30.46	159	303	7.1	166	91	46	99	0.65	24	1	2	2	7	7.6	7.1

fbsd1	fbsd2	fbsd3	ppbsd1	ppbsd2	ppbsd3	sysbpd1	diasbpd1	sysbpd2	diasbpd2	sysbpd3	diasbpd3	ldld1	ldld2	ldld3	cardrisk
												127	124	133	4.1
120	132	138	163	161	181							143	105	90	10
100	92		140	130		120	80	110	80			92	101		
															1.3
119			98			120	70								3.5
136	189	181	315	242	299									78	3.1
93	98	117	110	163	156	120	80	126	84	140	80	121	120	138	12.9
92	95		128	132		120	80	120	70			148	130		11.5
															1
												120	130	148	10.3
															7.4
107	112	104	192	160	132	120	70	130	80	130	70	117	108	98	13.5
150	160	141	214	200	220	130	80	140	70	140	90	130	122	120	
154	155	212	222	226	299	130	80	138	84	128	86	140	90	68	17.3
150	120	128	190	182	142	160	100	150	90	150	90	114	128	131	39.7
												128	156	139	6.4
												130	125	115	0.5
176	156	139	232	180	162							120	112	103	6.8
179	217	397	275	251	607							110	93	89	26.4
167	151	118	350	253	133	150	100	140	80	110	70	140	104	78	27.1
															0.5
															1.4
															5
180	156	152	290	299	238	140	100	130	80	120	76	150	138	121	18.9
												110	79	89	5.4
															1.7
												127	110	107	0.7
												140	130	121	16.2
103	114	123	175	105	148	120	70	130	80	120	70	93	70	85	18.9
148	129	110	188	202	140	140	80	130	78	130	84	163	111	101	
															3
															9.7
155	140	163	198	200	228							123	139	118	10.9
144	96	98	227	189	263							76	75	91	17.3
						150	100	140	90	140	90	140	121	131	15.8
						150	100	160	100	160	90				3.6
						150	90	140	80	130	90				8
												110	130	217	11.3
												130	126	57	5.5
236	180	204	310	260	222	150	90	140	90	140	80	110	100	77	16.8
130	120	105	170	160	156							142	122	111	12.7
242	210	205	408	300	323	140	88	130	90	130	90	172	140	152	10.5
120	116	110	156	136	180	150	88	140	90	140	80	176	110	99	14.8
127	246	166	366	159	303	140	90	150	94	130	84	150	120	99	13.6

ANNEXURE 8-STANDARD CRITERIA USED FOR DIAGNOSIS OF DISEASES OF INTEREST AND TREATMENT TARGETS.

TYPE2 DIABETES MELLITUS

American Diabetic association 2015 guidelines

A1C ≥6.5%*

(Performed in lab using NGSP-certified method and standardized to DCCT assay)

FPG ≥126 mg/dL (7.0 mmol/L)*

Fasting defined as no caloric intake for ≥8 hrs

2-hr PG ≥200 mg/dL (11.1 mmol/L) during OGTT (75-g)*

Performed as described by the WHO, using glucose load containing the equlivalent of 75g anhydrous glucose dissolved in water

Random PG ≥200 mg/dL (11.1 mmol/L)

In persons with symptoms of hyperglycemia or hyperglycemic crisis

***In the absence of unequivocal hyperglycemia results should be confirmed using repeat testing**

TREATMENT GOALS

HbA1c ≤ 7 in non pregnant adults.

Or ≤ 6.5 in pregnancy or Type 1 diabetes

Fasting plasma glucose less than 126mg/dl

Post prandial plasma glucose less than 180mg/dl

SYSTEMIC HYPERTENSION

JNC 8 Guidelines for diagnosis

Age ≥60	SBP ≥150 mm Hg or DBP ≥90 mm Hg

Age ≤60	DBP ≥90 mm Hg
	SBP ≥140 mm Hg
Age ≥18 with CKD[†]	SBP ≥140 mm Hg or DBP ≥90 mm Hg
Age ≥18 with diabetes	SBP ≥140 mm Hg or DBP ≥90 mm Hg

Treatment goals would be to maintain blood pressures below the abovementioned levels.

DYSLIPIDEMIA

NCEP ATP III GUIDELINES- DIAGNOSIS AND TREATMENT GOALS

- **LDL Cholesterol - Primary Target of Therapy**

<100	**Optimal**
100-129	**Near Optimal/Above Optimal**
130-159	**Borderline High**
160-189	**High**
190	**Very high**

- **Total Cholesterol**

<200	**Desirable**
200-239	**Borderline High**

240	**High**

- **HDL Cholesterol**

<40	**Low**
>60	**High**

LDL Cholesterol Goals and Cutpoints for Therapeutic Lifestyle Changes (TLC) and Drug Therapy in Different Risk Categories

Risk Category	LDL Goal (mg/dL)	LDL Level at Which to Initiate Therapeutic Lifestyle Changes (TLC) (mg/dL)	LDL Level at Which to Consider Drug Therapy (mg/dL)
CHD or CHD Risk Equivalents (10-year risk >20%)	<100	≥100	≥130 (100–129: drug optional)
2+ Risk Factors (10-year risk ≤20%)	<130	≥130	10-year risk 10–20%: ≥130 10-year risk <10%: ≥160
0–1 Risk Factor	<160	≥160	≥190 (160–189: LDL-lowering drug optional)

CHRONIC KIDNEY DISEASE

Revised chronic kidney disease classification based upon glomerular filtration rate and albuminuria

GFR stages

GFR	(mL/min/1.73 m2)	
G1	>90	Normal or high
G2	60 to 89	Mildly decreased
G3a	45 to 59	Mildly to moderately decreased
G3b	30 to 44	Moderately to severely decreased
G4	15 to 29	Severely decreased
G5	<15	Kidney failure (add D if treated by dialysis)

Albuminuria stages

AER	(mg/day)	Terms
A1	<30	Normal to mildly increased (may be subdivided for risk prediction)
A2	30 to 300	Moderately increased
A3	>300	Severely increased (may be subdivided into nephrotic and non-nephrotic for differential diagnosis, management, and risk prediction)

GFR: glomerular filtration rate; AER: albumin excretion rate; CKD: chronic kidney disease; KDIGO: Kidney Disease Improving Global Outcomes.

Data from:

1. KDIGO. Summary of recommendation statements. Kidney Int 2013; 3 (Suppl):5.

2. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis 2002; 39 (Suppl 1):S1.

OSTEOPOROSIS

Test Results using DEXA	**Interpretation(WHO)**
T-score -2.5 and lower	**Osteoporosis**

T-score between -1 and -2.5	**Osteopenia**
T-score -1 and higher	**Normal**
Z-score -2.0 and lower	**Below expected range for age**
Z-score above -2.0	**Within expected range for age**

Bone density - assessed by dual energy X-ray absorptiometry (DEXA)

ISCHAEMIC HEART DISEASE

ECG changes suggestive of ischaemia and/or treadmill test positivity in patients who are symptomatic or have ECG changes.

CEREBROVASCULAR DISEASE

Previous history of the same or evidence in the form of residual deficits or previous imaging will be considered

LIPODYSTROPHY

Trunk fat/lower limb fat mass ratio >2.28 identified 54.3% of patients with HIV receiving HAART as having lipodystrophy and had the highest odds ratio for predicting metabolic syndrome; based on a previous study conducted in our institution which developed an objective definition of HIV associated lipodystrophy using regional fat mass ratios.(75)

Hence trunk fat/lower limb fat mass ratio more than 2.28 is taken as as cut off for defining lipodystrophy..

METABOLIC SYNDROME-NCEP ATP III GUIDELINES

Any three (or more) of the following factors constitute a diagnosis of metabolic syndrome:

- **Increased waist circumference: ethnicity specific - eg, Caucasian men ≥94 cm and women ≥80 cm; South Asian men ≥90 cm and women ≥80 cm.**
- **If body mass index is over 30 kg/m^2, central obesity can be assumed and waist circumference does not need to be measured.**
- **Raised triglycerides:**
    - **>150 mg/dL (1·7 mmol/L)**
    - **Or specific treatment for this lipid abnormality**
- **Reduced HDL-cholesterol:**
    - **<40 mg/dL (1·03 mmol/L) in men**
    - **<50 mg/dL (1·29 mmol/L) in women**
    - **Or specific treatment for this lipid abnormality**
- **Raised blood pressure:**
    - **Systolic ≥130 mm Hg**
    - **Diastolic ≥85 mm Hg**
    - **Or treatment of previously diagnosed hypertension**
- **Raised fasting plasma glucose:**
    - **Fasting plasma glucose ≥100 mg/dL (5·6 mmol/L)**

Central obesity(WHO classification for Asians):

Waist circumference >= 90cm in men and >=80cm in women.

General obesity (WHO classification for Asia-Pacific region):

1. **Under weight: BMI <18.5Kg/M^2**
2. **Normal: BMI 18.5 to 22.9Kg/M^2**
3. **Overweight: BMI 23 to 24.9Kg/M^2**
4. **Obese class I: BMI 25 to 29.9Kg/M^2**
5. **Obese class II:BMI ≥ 30Kg/M^2**

(Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis

Society; and International Association for the Study of Obesity. Circulation. 2009 Oct 20;120(16):1640-5.)

SMOKING STATUS

(Canoy D, Wareham N, Luben R, Welch A, Bingham S, Day N, et al. Cigarette Smoking and Fat Distribution in 21, 828 British Men and Women: A Population-based Study. Obes Res. 2005 Aug 1; 13(8):1466–75**.)**

a) **Current smokers: Smoking at present.**

b) **Former smokers : Not smoking at present but had previously smoked one cigarette a day for atleast a year**

c) **Never smokers: Smoked neither at present nor in the past.**

One smoking pack year will be equivalent to one cigarette pack per day for one year.

ALCOHOL CONSUMPTION

(Dorn JM, Hovey K, Muti P, Freudenheim JL, Russell M, Nochajski TH, et al. Alcohol Drinking Patterns Differentially Affect Central Adiposity as Measured by Abdominal Height in Women and Men. J Nutr. 2003 Aug 1;133(8):2655–62, Schroder et al : The relationship between waist- to-hip ratio and occupational status and life-style factors among middle aged male and female Japanese workers)

(a) Lifetime abstainer: Never had 12 or more drinks in their lifetime or in any 1 year period.

(b) Noncurrent drinker: Previously consumed 12 or more drinks in their lifetime or in any one-year period, but did not consume any alcohol in the previous 30 days.

(c) Current drinker: Consumed at least one alcoholic beverage in the 30 days before the interview.

Alcohol intake in grams will be calculated by multiplying the amount of beverage consumed in milliliters with the grade (percentage) of alcohol and the constant 0.80 to transform alcohol volumes into weight. 11% for wine, 5% for beer and 40% for spirits are the defined grades.